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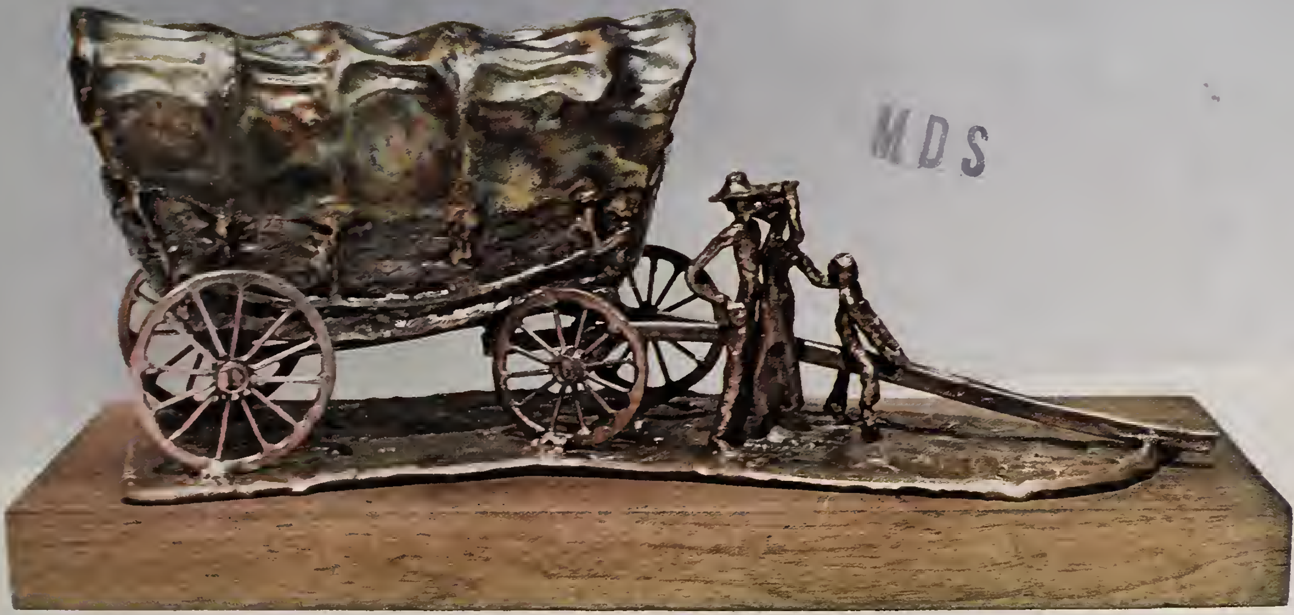
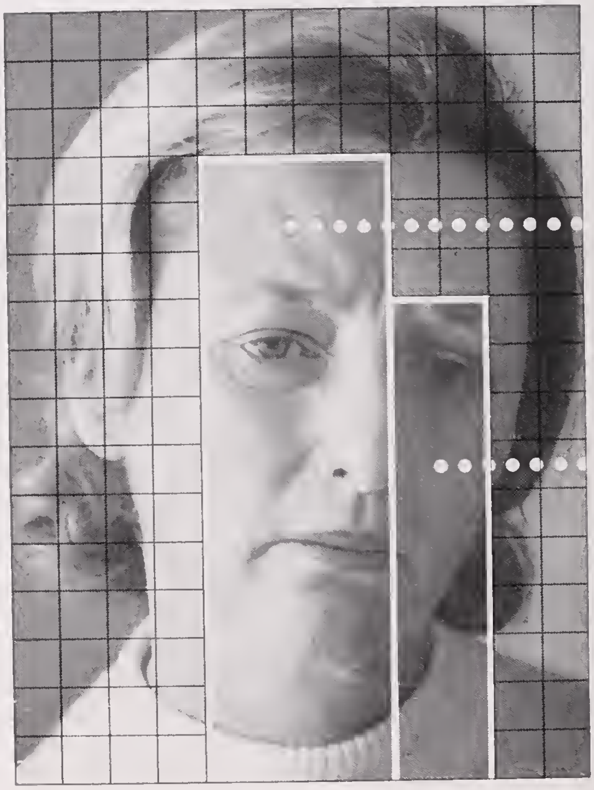


ney's End"

Don L. Carlon, M.D.

JANUARY 1976

Both ofte


Predominant psychoneurotic anxiety
Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in fre
and/or severity of grand mal seizu
require increased dosage of standa
convulsant medication; abrupt wit
may be associated with temporary
crease in frequency and/or severit
seizures. Advise against simultane
gestion of alcohol and other CNS d
sants. Withdrawal symptoms (simi
those with barbiturates and alcoho
occurred following abrupt disconti
(convulsions, tremor, abdominal a
cle cramps, vomiting and sweating
addiction-prone individuals under

respond to one

According to her major
ptoms, she is a psychoneu-
patient with severe
iety. But according to the
ription she gives of her
ngs, part of the problem
sound like depression.
is because her problem,
ough primarily one of ex-
ive anxiety, is often accom-
ed by depressive symptom-
ogy. Valium (diazepam)
provide relief for both—as
xcessive anxiety is re-
d, the depressive symp-
s associated with it are also
relieved.
There are other advan-
s in using Valium for the
agement of psychoneu-
anxiety with secondary
essive symptoms: the
hotherapeutic effect of
um is pronounced and
d. This means that im-
ement is usually apparent
in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

Valium® (diazepam) Ⓘⓥ

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

illance because of their predisposi-
o habituation and dependence. In
ancy, lactation or women of child-
ng age, weigh potential benefit
st possible hazard.
utions: If combined with other psy-
opics or anticonvulsants, consider
ully pharmacology of agents em-
d; drugs such as phenothiazines,
tics, barbiturates, MAO inhibitors
ther antidepressants may potentiate
tion. Usual precautions indicated in
nts severely depressed, or with latent
ssion, or with suicidal tendencies.
Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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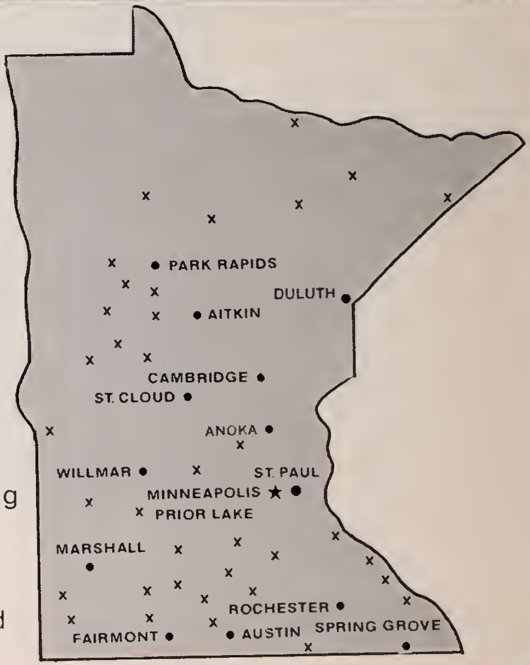
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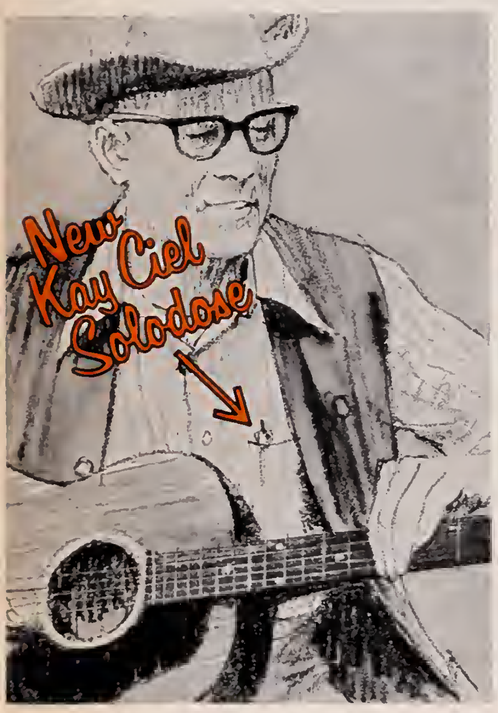
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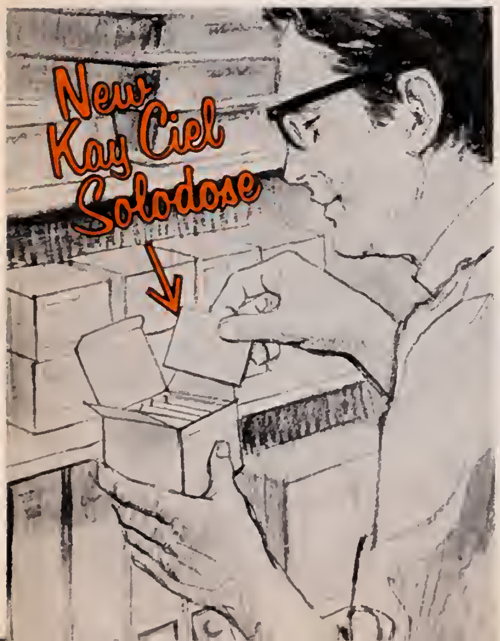
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President's Letter

The Non-System

During the last ten years, the delivery of medical care has been attacked repeatedly as a non-system. It has been likened to a cottage industry that prevailed prior to the industrial revolution. Some of our politicians and health planners would prefer to replace it with a structured integrated bureaucratic system with echelons of bureaucrats in command at every level of a pyramidal system. In fact, many of the programs implemented and proposed by the health planners have made subtle and not so subtle changes in health care delivery. However, the non-system has remained fairly intact and adjusted to Medicare, Medicaid, PSRO and RMP programs. The National Health Planning and Resources Development Act of 1974, which is now being implemented, looms as a potential threat to destroy the non-system for delivery of medical care that has served our nation so well.

We are told that the federal programs in health enacted by Congress are now too expensive, and in the interests of economy more bureaucratic control and planning are necessary to cut and hold down federal spending. It is, indeed, tragic that Congress has not heeded the warnings given by organized medicine, since Medicare was first proposed that many of these programs would be much more costly than the politicians believed and that some of the programs were either not needed or unwise. A significant cost factor in all these programs is the administration and bureaucracy that grows with the program.

I believe that our non-system of health care delivery which was not perfect and had some deficiencies was far superior to what the planners are now proposing. If and when the non-system is replaced, I propose the following: a program that permits the needy and disadvantaged to get medical care with dignity; an insurance program that permits out-patient treatment and examination without penalty in benefits for the patient; a program that encourages a variety of systems of health care delivery without subsidization of any particular program; a program that allows a physician to treat patients according to Hippocratic principles and without fear of litigation when defensive medicine is not practiced; a program that allows a physician freedom to practice the art of medicine; and a program that denies the politician and the health planner the making of medical decisions. A free people should have a health care system that is free of the bureaucratic controls and costs proposed by the planners—even if it is a non-system.

GRDiessner

G. Roy Diessner, M.D.
President
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Editor's Notebook

Social and Economic Articles

Each time I attend a Minnesota Medical Association function, at least one physician approachs me and asks, usually with heat: "What about more socio-economic articles?" I try to calm the questioner by saying social and economic articles are welcome in MINNESOTA MEDICINE, as indeed they are.

Consider, for example, this issue. Here you will find four articles or items relating to social and economic issues: (1) "Encroachment on the Private Practice of Medicine" (page 25); (2) "Inflation and Medicine 1954-1974" (page 33); (3) "Heroics in Medicine" (page 34); and (4) "Resection of Rhabdomyosarcoma of the Neck—An Office Procedure" (page 24). The title of the last article hardly suggests anything about society or economics. But when you read it, you will discover it has a great deal to do with both.

Still, I suppose, suspicion will persist that we do not like social and economic articles. Part of that suspicion may be because of our editorial policy that a social and economic article ought to be as well written as a scientific article. Any article, no matter what the subject matter, ought to have an appropriate title, say something new, stick to the facts, support its reasoning with evidence, hang together, and have the right tone.

What do I mean by "tone"? Well, the article ought not to be blatantly partisan, strident, or opinionated. Not that we mind a person expressing an opinion. We welcome articles that let the reader know exactly where the writer stands. But we like articles with a sense of reason and proportion, rather than articles that read like pamplets, tracts, or campaign literature.

How can one avoid partisan prose? I'm not precisely sure, but I like George Orwell's set of rules from "Politics and the English Language."* Orwell sets forth these rules as a means of "cutting out . . . stale and mixed images, all prefabricated phrases, needless repetitions, and humbug and vagueness generally."

"(i) Never use a metaphor, simile, or other figure of speech which you are used to seeing in print.
(ii) Never use a long word where a short one will do.
(iii) If it is possible to cut a word out, always cut it out.
(iv) Never use the passive where you can use the active.
(v) Never use a foreign phrase, a scientific word, a jargon word if you can think of the everyday English equivalent.
(vi) Break any of these rules sooner than say anything outright barbarous."

In the main, the purpose of this editorial is to encourage you to submit material on social and economic issues. Write an article. Compose a letter to the editor. Ask for articles on specific subjects. We, in our turn, will be doing a few things on our own. For example, we plan to publish a few interviews with Minnesota Medical Association leaders, and we may create a new page to acquaint you with the latest legislative news.

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*Shooting an Elephant, Harcourt, Brace, 1950.

This opening of our pages to let in more social and economic material does not mean we will change our editorial standards. We shall continue to reject poor or inappropriate papers. At the same time, this opening does mean we recognize the physician's role in society is changing. Physicians will and should participate more in society's activities, defend their positions before other segments of society, and anticipate what society wants from us. The physicians of Minnesota are, of course, aware of all this, or our leaders would not have gone to the trouble of forming a new division for the Minnesota Medical Association—the Department of Socioeconomic and Legislative Affairs.

This is not a social, economic, or legislative journal. It is a medical journal. But any editor worth his salt, especially a medical editor, should spend a good deal of his time finding out what readers want. I sense thoughtful readers want to know what's going on outside the profession, as well as inside.

Richard L Reece MD

Minnesota State Medical Association Annual Meeting

Be preregistered!

Working on the principle that two seminars are better than one general session, the Scientific Assembly Subcommittee devised a program format which provides a large number of physicians with the learning atmosphere of the controlled attendance session. And though we would like to take credit for the entire program concept, we owe thanks to those members who completed evaluation cards at last year's Annual Meeting.

The cards submitted not only told us what was wrong with last year's meeting but offered constructive criticism for planning CME '76. Evaluations indicated that more sessions encouraging question and answer periods were wanted; that seminars severely restricted members attending sessions of interest to all; that although general sessions granted attendance to many, their learning advantages were limited. Thus, six seminars will be presented morning and afternoon on Thursday and Friday. Twelve topics will be offered to satisfy a variety of educational tastes as well as certify physicians in CPR.

Members will be getting the best of last year's Meeting—and a lot more; But there is one hitch. Since all attendance is limited, you must be preregistered to be admitted to any of the seminars. Registration materials will be in the mail in March. Select the programs you wish to attend and return the form as soon as possible. Remember, the earlier the form is returned, the better your chances of getting your first choices.

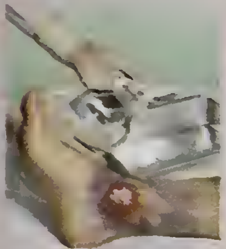
Just as "Be prepared" is the motto of the Boy Scouts, "Be preregistered" will be the maxim for CME '76!

R. D. Semsch, M.D.
Chairman
Scientific Assembly

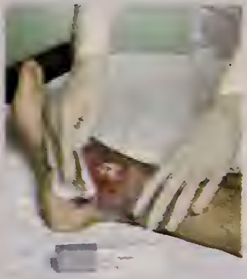
adjunctive therapy for wound debridement

HELPS TO REMOVE:
- Necrotic Tissue and Associated Odor

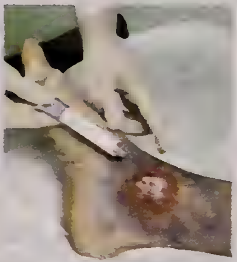
HELPS PREPARE WOUND FOR:
- Granulation/Healing
- Granulation/Grafting



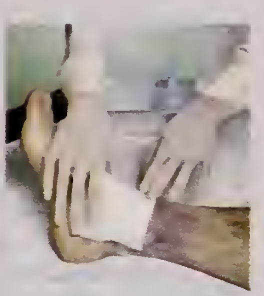
CLEANSE WOUND
Thoroughly cleanse and irrigate wound area with sodium chloride or water solutions. Wound MUST be cleansed of antiseptics or heavy-metal antibacterials.



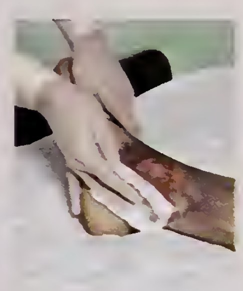
THOROUGHLY MOISTEN
Thoroughly moisten wound area either through tubbing, showering, or wet soaks (e.g., sodium chloride or water solutions).



APPLY ENZYME
Apply a layer of TRAVASE Ointment. Assure intimate contact with necrotic tissue and complete wound coverage.

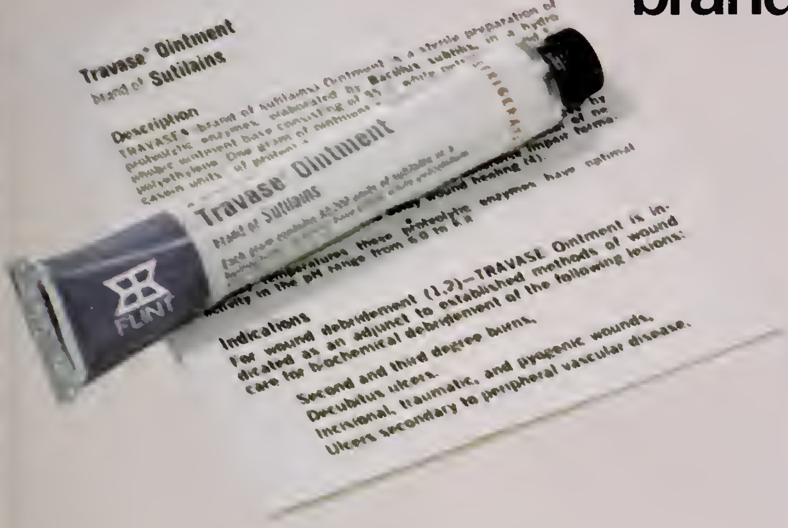


APPLY MOIST DRESSING
Apply loose moist dressings (most important with dry leathery eschar).



CHANGE DRESSINGS
When changing dressing, gently wipe away the dissolved material. Repeat the procedure, including application of TRAVASE Ointment, 3 to 4 times per day for best results.

Travase® Ointment
brand of Sutilains



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Description

Indications
For wound debridement (1,2)—TRAVASE Ointment is indicated as an adjunct to established methods of wound care for biochemical debridement of the following lesions:
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ulcers

TERRY V. CARLE M.D., CLINICAL INSTRUCTOR, DEPT. OF PHYS. MED. & REHAB.,
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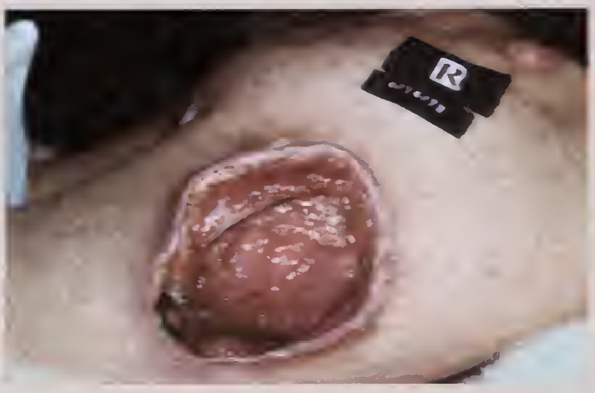
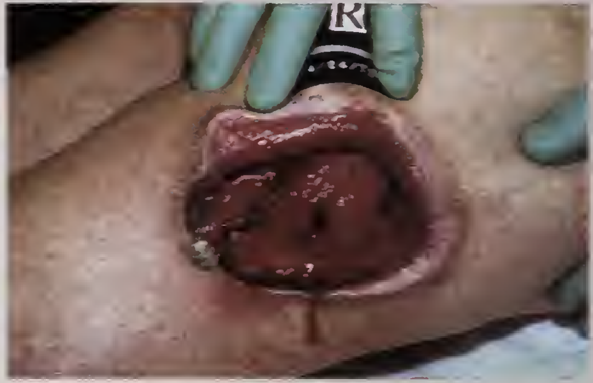


Before treatment, necrotic matter coated the inner surfaces of this decubitus ulcer.



After six days of TRAVASE therapy, debridement is nearly complete and granulation evident.

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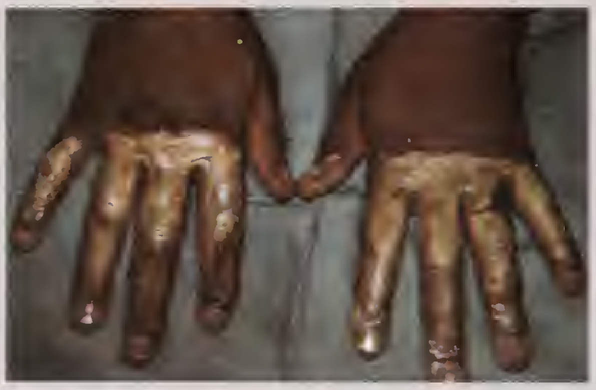
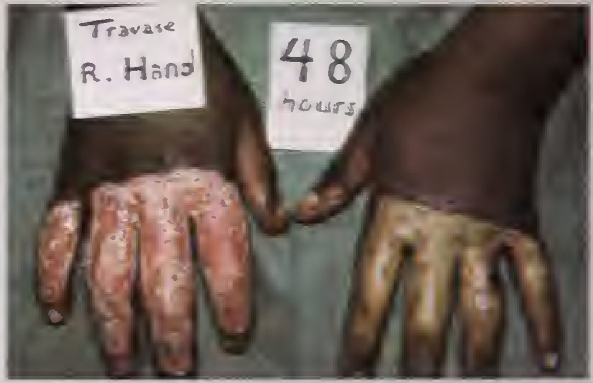
burns

DALE B. DUBIN, M.D., DIPLOMATE,
AMERICAN BOARD OF PLASTIC SURGERY, TAMPA, FLORIDA



Before treatment . . .



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ontents—January, 1976

VER PHOTOGRAPH—"Journey's End"
Don L. Carlon, M.D. ... 37

ESIDENT'S LETTER—The Non-System
G. Roy Diessner, M.D., President ... 5

ITOR'S NOTEBOOK—About Socio-Economic Articles
Richard L. Reece, M.D., Editor-in-Chief ... 7

IGINAL CONTRIBUTIONS

Diagnostic Surgical Exploration for Renal Masses
David H. Kauder, M.D. and William C. DeWolf, M.D. ... 13

Functional Dermatochalasia
Richard P. Carroll, M.D. ... 15

Clinical Effects of Warm Ischemia and Prolonged Preservation on the Outcome of Transplanted Kidneys
Luis H. Toledo-Pereyra, M.D. et al. ... 18

Resection of Rhabdomyosarcoma of the Neck—An Office Procedure
Harrison H. Farley, M.D. ... 24

ITORIALS

Clinical Effects of Warm Ischemia and Prolonged Preservation on the Outcome of Transplanted Kidneys
Horst Zincke, M.D. ... 31

Functional Dermatochalasia
Robert R. Waller, M.D. ... 31

TTERS TO THE EDITOR

Inflation and Medicine 1954-1974
Howard D. Baker ... 33

ILOSOPHICAL MUSINGS OF A SURGEON
Heroics in Medicine
Carl O. Rice, M.D. ... 34

NNESOTA STATE MEDICAL ASSOCIATION—Annual Meeting
R. D. Semsch, M.D. ... 8

ECIAL ARTICLE—Encroachment on the Private Practice of Medicine
Stuart V. Thorson, M.D. ... 25

RAY CONFERENCE—Diarrhea in a Patient with Renal Failure
S. H. Tsai, M.D. and Kenneth Preimesberger, M.D. ... 35

REENING—School Screening for the Early Detection of Spine Deformities
John E. Lonstein, M.D. et al. ... 51

ACTURE CONFERENCE—Cast Bracing of Femoral Fractures
Stephen H. McCoy, M.D. et al. ... 58

OK REVIEWS ... 39

NTINUING EDUCATION ... 17, 26, 32 57, 66

MEMORIAM ... 45

ASSIFIED ADVERTISEMENTS ... 50

DEX TO ADVERTISERS ... 66

Volume 59, 1
Pages 1-66

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Diagnostic Surgical Exploration for Renal Masses

DAVID H. KAUDER, M.D.* and WILLIAM C. DeWOLF, M.D.*

The evaluation of renal masses is often difficult. Modern diagnostic methods yield a high degree of accuracy but occasionally fail. Surgical exploration should be considered a diagnostic, as well as therapeutic, modality.

DIAGNOSTIC SURGICAL exploration is being replaced by less invasive radiologic techniques, such as, nephrotomography, arteriography, and cyst puncture in the evaluation of renal masses. These ests may be inaccurate from one to five percent of the time. The indications, value, and purpose of diagnostic surgical exploration needs re-emphasis and will be discussed in the following paper.

Case Report

A 44-year old white male was admitted for evaluation of a renal mass. Physical examination and laboratory data including hemogram, urinalysis, chest radiograph, and SMA 12 all were normal. An intravenous urogram showed a left renal mass with circumlinear calcification (Figures 1 and 2). Comparison with roentgenograms taken three years previously showed no change. A selective left renal arteriogram with epinephrine studies showed no tumor vessels (Figure 3). Despite the absence of hematuria, stable size of the renal mass and no tumor vessels, the presence of calcification raised the suspicion for malignant disease. The patient was taken to surgery and a multi-loculated cyst with both clear and blood tinged fluid was found. A radical nephrectomy

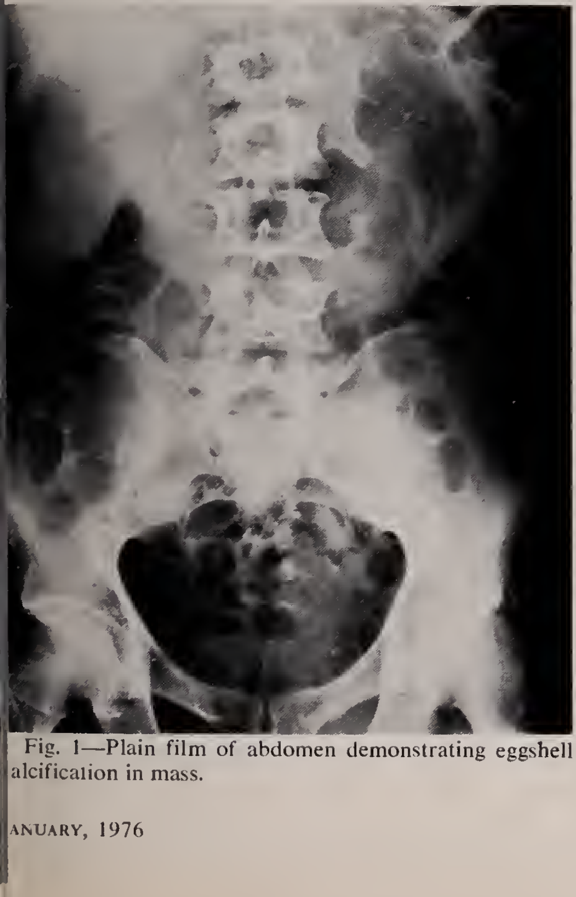
Fig. 1—Plain film of abdomen demonstrating eggshell alcification in mass.

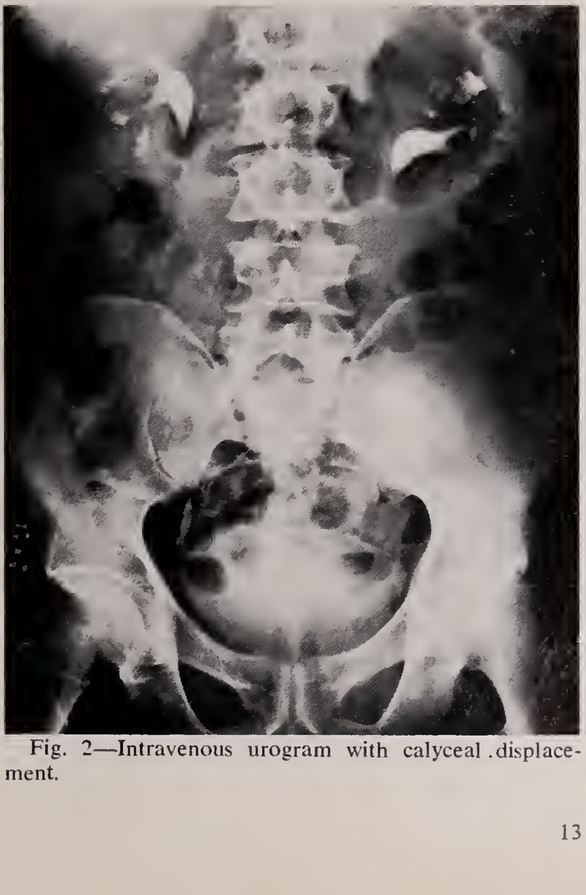
Fig. 2—Intravenous urogram with calyceal displacement.

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*Department of Urologic Surgery, University of Minnesota, Health Sciences Center, Minneapolis, Minnesota, and Division f Urologic Surgery, Veterans Administration Hospital, Minneapolis, Minnesota.

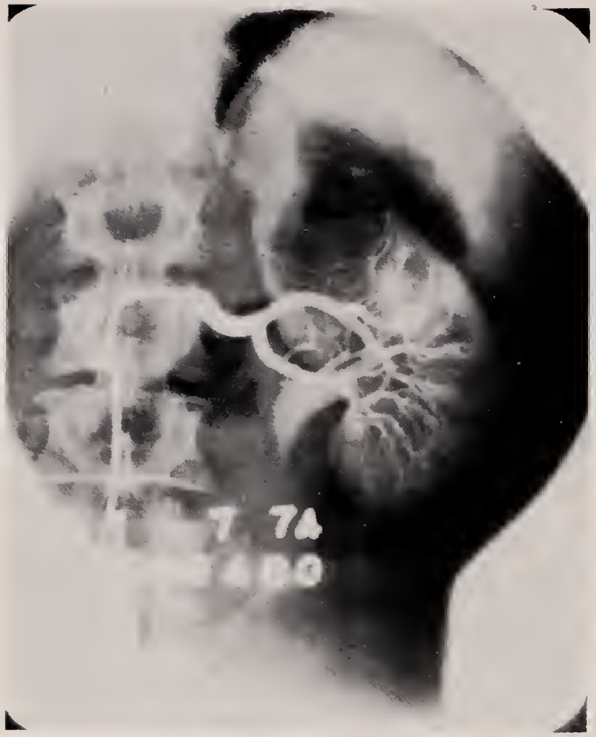

Fig. 3—Selective renal arteriogram showing avascular mass.

was performed which revealed hypernephroma along the border of a cyst. All associated lymph nodes were negative for tumor. Postoperatively the patient did well and at followup 18 months later is disease free.

Discussion

The evaluation of renal masses is often difficult. Sonography has been used to differentiate cystic from solid lesions. The correlation of radiographic findings with surgery has shown the routine intravenous urogram to be approximately 50 percent accurate.[2] Nephrotomography has increased the diagnostic accuracy of the routine intravenous urogram to 56-95 percent,[2,3] while arteriography has correctly predicted the surgical diagnosis in 88-97 percent of those cases reported.[2,3] Finally, cyst puncture which, when interpreted in light of cytologic and biochemical analysis of the aspirated fluid may yield a diagnostic accuracy of 97 percent.[1,2]

Our case illustrates the spectrum of non-invasive analysis, and points to the value of diagnostic surgical exploration. The preliminary preoperative evaluation resulted in presumptive evidence for benign disease: (1) The urinalysis was normal. (2) The intravenous pyelogram revealed a mass which, when compared with old films, was found to be unchanged in three years; this is considered by some to be strong evidence for a benign process.[6] (3) The mass contained eggshell calcifications which has been reported to be associated with a benign process.[7] (4) Arteriography with associated epinephrine studies did not show evidence for tumor. Cyst puncture may have been beneficial in this case; however, calcification has been considered a relative contraindication to cyst puncture.[4] Circumlinear calcification may represent a problem with cyst puncture because of its association with vascular calcifications. The presence of calcification raised our index of suspicion for malignancy and surgical exploration was performed. Hypernephroma was found.

Proponents for diagnostic surgical exploration point to the 1 to 7 percent incidence of the coexistence of tumor within a cyst.[8-10] Occasionally, hypernephroma can occur within the free cyst wall with no infiltration of the inner lining or staining of the cyst fluid.[11] Such cases are diagnosed only by surgical exploration. The disadvantage of surgical exploration is the associated morbidity and mortality. Kropp and Grayhack[12] listed a mortality of 0.8 percent and a major morbidity of 2.3 percent. Because of the increased morbidity with older age groups, cyst puncture should be given serious consideration to replace surgical exploration.

Which cases need *diagnostic* surgical evaluation? Strong consideration for such a procedure should be made: (1) in those cases which do not lend themselves to cyst puncture (anatomic position or size); (2) when presumptive signs of malignancy exist, i.e. hematuria; (3) those cases in which cyst puncture results are inadequate; (4) in those calcified renal masses with a "negative evaluation;" and (5) in younger patients in whom surgical risk is minimal and complete diagnosis is to be obtained.

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8-14. Will be found on page 23.

Functional Dermatochalasia

RICHARD P. CARROLL, M.D.*

It is important for physicians to realize that blepharoplasty does not automatically imply cosmetic surgery. The patient with functional dermatochalasia is neither primarily interested in cosmetic improvement nor is the surgery performed for that reason. These patients have disabling symptoms that coincidently require a surgical procedure that is used for aesthetic purposes in another group of patients.

THE BAGGY EYELID is generally considered a cosmetic impairment. There are, however, many individuals with dermatochalasia who are not bothered by the cosmetic aspects of this problem, but rather have disabling symptoms. These patients most frequently come to the ophthalmologist, but they may first seek relief of their symptoms from the general practitioner, the internist, or other medical or surgical specialists. It is important for the ophthalmologist as well as his colleagues to identify these individuals so that specific therapy may be instituted and costly, unnecessary, and sometimes dangerous diagnostic procedures may be avoided.

The patient with functional dermatochalasia is usually over 50 years of age, and most frequently complains of brow aching. This may be described by the patient as eyestrain, headache, or a heaviness over the eyes. Most likely the source of these symptoms is over-worked frontalis muscles. To maintain an adequate visual field in spite of drooping eyelids, it is necessary for these individuals to maintain a sustained frontalis contraction that gives rise to the patient's symptoms.

Unlike the younger patient who requests treatment for dermatochalasis for aesthetic reasons, patients with functional dermatochalasia are usually unaware of, or at least unconcerned about, their baggy eyelids. They seldom associate their symptoms with their dermatochalasia, and often attribute their brow aching to needing a change in glasses, a recurrent sinus problem, or everyday tension. Old photographs are useful in documenting to the patient the development of his baggy lids and their relationship to his symptoms.

Tearing and eye irritation are frequent complaints in older individuals and dermatochalasia may be the cause of these symptoms. Excess upper lid skin can invert the lid margin, causing the lashes to rub upon the globe. Both the inturned margin and the tearing and irritation in these patients will, of course, be refractory to traditional therapy for these conditions.

Other patients with functional dermatochalasia will complain of visual field impairment. An extreme case is shown in Figure 1. More frequently, the upper temporal field is obstructed by a curtain of upper lid skin that may or may not be associated with drooping eyebrows. Such field defects cause difficulties in ambulation as well as in driving for the elderly patient, presenting an additional hazard to a person who may already be somewhat slowed in his physical responses. A series of mishaps while driving brought the

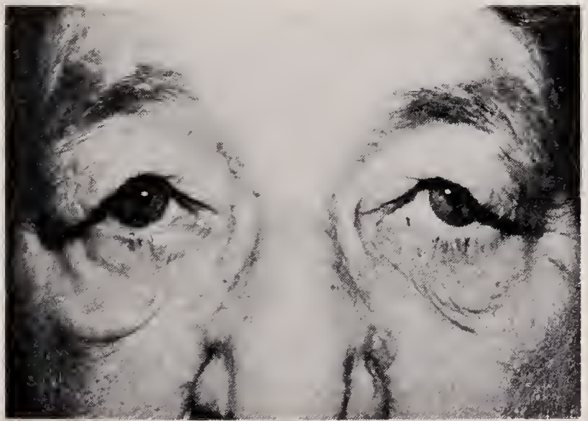
Fig. 1—68-year-old female with severe functional dermatochalasia and associated brow droop.

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*St. Paul, Minnesota.
See editorial, page 31.

woman shown in Figure 1 to the attention of her ophthalmologist.

Evaluation

Evaluation of the patient with functional dermatochalasia should include a thorough inquiry into the patient's past ocular and general medical history. More specifically, general systemic causes of baggy eyelids such as chronic renal disease, various collagen diseases, and thyroid problems can simulate dermatochalasia. Such underlying systemic causes must be identified and referred for appropriate evaluation and indicated treatment prior to performing blepharoplasty.

Local ocular conditions may either simulate or accompany dermatochalasia. What appears at first inspection to be an excessive amount of skin in the upper lid may be primarily due to a herniation of orbital fat through the orbital septum. There are two fat pockets in each eyelid. To avoid an inadequate result, the offending herniated fat must be removed in addition to the excess skin. Fat herniation is likely to be most prominent in the medial pockets, and it can be removed from these pockets with minimal risk. Removal of fat from the temporal pockets, however, may result in damage to the levator muscle or a deep supratarsal sulcus. Gentle pressure on the globe by the examiner will cause herniated orbital fat pockets to become more prominent. This technique is useful preoperatively to identify herniation of orbital fat, and during surgery to aid in its proper removal.

Occasionally a bulge will be noted in the temporal aspect of the upper lid caused by a herniated lacrimal gland. This bulge should not be mistaken for herniated orbital fat and should not be removed. The herniated lacrimal gland should be sutured to the periosteum of the lacrimal fossa.

Frequently patients with functional dermatochalasia will have an associated drooping of the temporal one-half of their eyebrow that contributes to their baggy eyelids. By simply elevating the eyebrows with his thumb, the examiner can often eliminate a significant amount of the bagginess. Obviously the primary target of surgery in these patients should be the eyebrows rather than the skin of the eyelid, although usually some skin must also be resected. Such a patient frequently gets little or no improvement from blepharoplasty alone. Figure 2 illustrates a patient with severe brow ptosis six months after undergoing an upper lid blepharoplasty. Figure 3 shows how elevation of his eyebrows almost eliminates his drooping eyelids. This man should have had a brow lift in addition to his blepharoplasty.

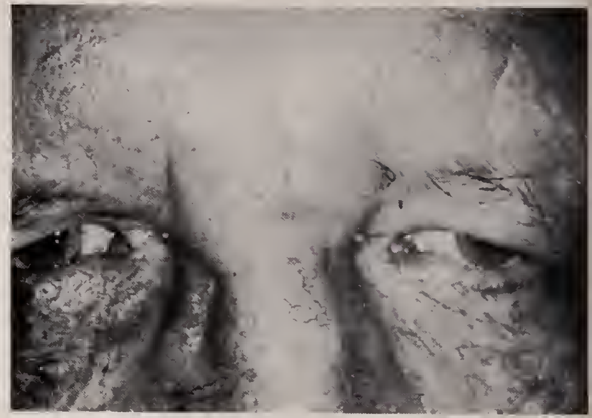

Fig. 2—72-year-old male who six months before this photograph had excess skin removed from both upper lids. His disability persisted postoperatively because his severe brow droop was unrecognized.

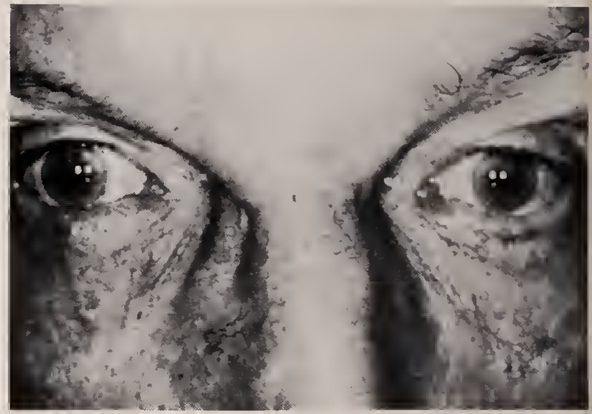

Fig. 3—The same gentleman shown in Figure 2 with the examiner manually elevating his brows. He needs a bilateral brow lift to correct his disability.

A varying amount of ptosis sometimes accompanies functional dermatochalasia. Recognition of this accompanying condition is very important since resecting skin from the eyelids will usually not elevate a drooping eyelid. Careful attention to the position of the eyelids once the weight of the excess skin and eyebrows has been eliminated by the examiner will enable the examiner to detect co-existent degenerative ptosis.

Treatment

As in all types of reconstructive surgery, it is necessary that the patient be aware of what the problem is and what the surgeon plans to do about it. After the physician has made his determinations, it is helpful to have the patient hold a mirror in front of himself while the examiner demonstrates the particular problem. For example, if the brows are drooping, it is helpful to show the patient what elevation of the eyebrows does to his condition. The patient will then be able to readily understand why the surgeon is operating on his eyebrows as well as his eyelids to correct his baggy eyelids.

Just as the patient with functional dermatochalasia differs from the patient with cosmetic dermatochalasia, so does the goal of treatment differ in these two categories. The primary objective of treatment in patients with functional dermatochalasia is relief of troublesome symptoms rather than aesthetic perfection. Cosmetic improvement in these patients is a secondary benefit of surgery, and the patient should be so advised preoperatively. Keeping these objectives in mind, the surgeon should develop a conservative approach toward this group of patients, thereby effectively eliminating the most frequent complications of upper lid blepharoplasty.

Scarring following upper lid blepharoplasty is usually not a significant problem. Brow incisions, on the other hand, will almost always leave a noticeable scar. The patient should be aware of this fact preoperatively. It is possible to minimize these scars by placing brow incisions in natural forehead skin folds and by judicious use of makeup.

When a ptosis operation is done in conjunction with the blepharoplasty, the elevation is not always apparent in the immediate postoperative period. The patient should know that the final results of surgery may not be apparent for six to eight weeks after his operation.

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Clinical Effects of Warm Ischemia and Prolonged Preservation on the Outcome of Transplanted Kidneys

LUIS H. TOLEDO-PEREYRA, M.D.*, CLIVE O. CALLENDER, M.D.*,
ALLEN W. MOBERG, M.D.*, RICHARD L. SIMMONS, M.D.* and
JOHN S. NAJARIAN, M.D.

One hundred and seventy-eight potential cadaver kidneys in a period of 32 months were preserved by hypothermic pulsatile perfusion at the University of Minnesota. One hundred and forty-seven (82%) of these kidneys were transplanted; the rest were eliminated mainly because of nonavailable recipients (6%) and warm ischemic damage (6%). We report here on 111 kidneys that were transplanted at this medical center. Seventy-one kidneys (64%) functioned immediately, 36 kidneys (32%) had delayed function and four kidneys (4%) never functioned. There was a direct relationship between warm ischemic damage, long-term preservation, and acute tubular necrosis. Warm ischemia and prolonged preservation did not significantly affect the late function of the transplanted kidneys. Cadaver kidney use in our program depended basically on perfused organs. These were obtained from donors at our hospital and other community or city hospitals. Organ-sharing with other institutions was an important factor in our organ procurement center.

WE HAVE PREVIOUSLY reported on factors determining early kidney function after clinical preservation.[12] We found that warm ischemia and prolonged preservation had the most adverse effects upon cadaver kidneys after transplantation.[11,12] In this study we further analyze the effects of ischemia and length of preservation on the immediate function of perfused and transplanted kidneys.

Material and Methods

Within 32 months, 178 potential kidney grafts were obtained from 89 cadaver donors with irreversible brain damage as a result of accident (76%) or natural disease (24%) (Figure 1). Normal urinalysis, blood urea nitrogen, creatinine, electrolytes, blood sugar, two-hour creatinine clearance, and a negative clinical history of cancer, tuberculosis, diabetes mellitus, and septicemia were considered in evaluating the cadaver donor. Adequate levels of fluids were administered to the donor to maintain stable central venous pressure and urinary output before surgery. Bilateral nephrectomies were performed by the Donor Team according to standard techniques. During the op-

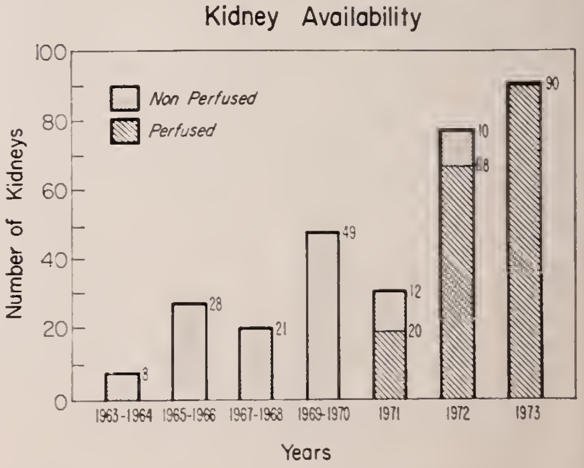

Fig. 1—There was a progressive increase of available cadaver donors up to 1973. Since the introduction of perfusion techniques (1971) practically all kidneys were perfused.

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*Department of Surgery, University of Minnesota Health Sciences Center, Minneapolis, Minnesota. Supported by USPHS Grant 5-PO2-AM 13083.

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See editorial, page 31.

erative procedure, most of the donor patients received furosemide (0.5-2.0 mg/kg), methylprednisolone (30 mg/kg), and in some cases phenoxibenzamine (1 mg/kg). Some patients also received 20 mg/K intravenously of antilymphocyte globulin (ALG) at the beginning of the operation. After nephrectomy, the kidneys were flushed with 4°C Ringer's lactate with heparin (10,000 U/L) and procaine (0.1 gm/L), until the venous effluent was clear. Immediately thereafter, the kidneys were placed in the Minnesota Mox-100 perfusion system*[4] at a systolic perfusion pressure of 60 mmHg, $PO_2$200 mmHg, osmolarity 280 mOsm, pH 7.4, temperature 7°C. Cryoprecipitated plasma (CPP) was used as the regular perfusate,[5] except for three kidneys that were perfused with human salt poor albumin (Cutter Laboratories). Both perfusates contained regular additives.[4,5]

The perfusate pressure, perfusion flow, blood gases, electrolytes, and lactic acid dehydrogenase (LDH) were determined at regular intervals during perfusion. All kidneys with a flow of less than 1.0 ml/min/gm, high perfusion pressure (>90 mmHg), and/or severe vascular abnormalities were eliminated for transplantation.

If the kidney had to be transported to another transplant center, it was kept in the transport module (Mox 100) until delivered. In some instances, the kidneys were kept in ice saline at 0°-4°C for several hours before transplantation.

The time that elapsed from the clamping of the renal artery (or absent blood pressure in the donor) until the kidney was first immersed in ice saline was recorded as the "warm ischemia" time. The period of kidney immersion in ice saline until the moment of revascularization in the recipient was recorded as the "cold ischemia" time.

Testing for histocompatibility was performed on peripheral blood donor lymphocytes or lymph nodes removed at nephrectomy. The recipients were selected on the basis of the histocompatibility matching. Transplantation of cadaver donor kidneys was performed by standard techniques. Postoperative function was followed by daily measurements of urine output and serum creatinine. A diagnosis of rejection was based on otherwise unexplained deterioration in renal function and the appearance of the renal biopsies. Acute tubular necrosis (ATN) or delayed function was diagnosed on those patients who had high creatinine, progressive deteriorating urine output and who required dialysis for variable periods of time. All patients that did not require dialysis were included in the immediate function group.

Results

One hundred and forty-seven (82%) of the potential kidneys were transplanted. Table 1 and Figure 2 list the reasons for not using the remaining 31 (18%) kidneys. Thirty-six kidneys were sent to other institutions, and 111 were transplanted at this University. The average preservation time for the kidneys grafted at this center was 20.6 hours (Figure 3). Thirty-six patients developed acute tubular necrosis (ATN) after transplantation and required one to six weeks of hemodialysis. Four patients had kidneys that never functioned because of technical problems or re-

TABLE 1
Renal Preservation: Clinical Experience
University of Minnesota
May 1971 — December 1973
(32 months)

Available Donors	89	
Available Perfused Kidneys	178	
Perfused Kidneys Transplanted	147	(82%)
U of M	111	(75%)
Shared	36	(25%)
Perfused Kidneys Not Used	31	(18%)
No Available Recipients	10	(6%)
Prolonged Warm Ischemia	10	(6%)
Technical Error Nephrectomy	5	(3%)
Anatomical Variation	4	(2%)
Perfusion Failure	2	(1%)

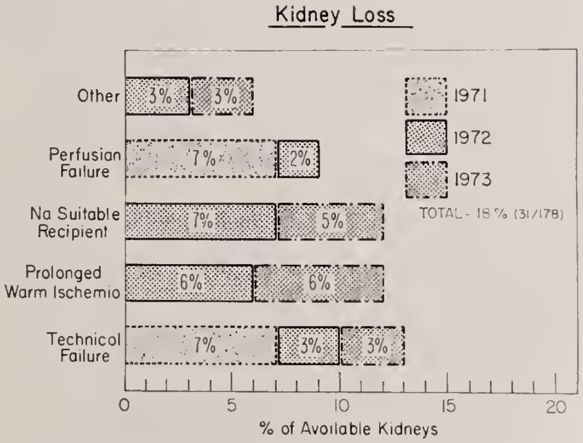

Fig. 2—A significant number of kidneys were not used for transplantation mainly because of prolonged warm ischemia and unavailable recipients. Technical failures and perfusion failures were also important causes. Eighteen percent of kidneys from the total group of kidneys were not used (kidney loss).

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†Waters Instruments Co., Rochester, Minnesota.

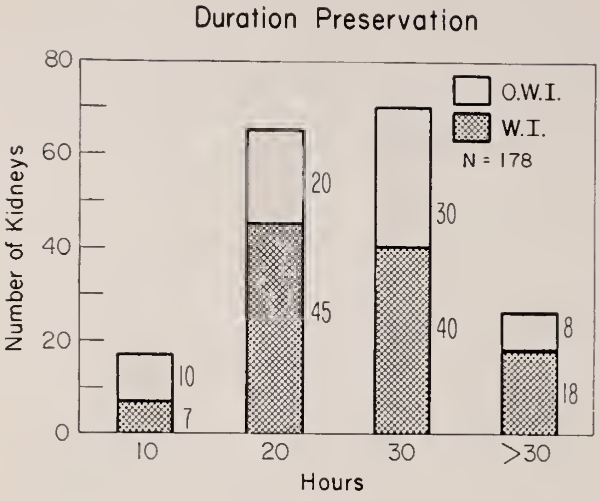

Fig. 3—Note that the average duration of preservation in the whole group of perfused kidneys was 20.6 hours. Sixty-two percent of all kidneys had some degree of warm ischemia (W.I.).

jection phenomenon (Table 2).

The average duration of preservation of the 36 kidneys that developed ATN after transplantation was 23.4 hours which was not significantly different when compared to the whole group of preserved kidneys. The average values of LDH in the perfusate of these kidneys that developed ATN was initially 75 U% and increased to values of 215 U% at the end of preservation. These values were not significantly different from the group of kidneys with the same time of preservation. Thus, there was no direct relationship between the LDH levels and the presence of ATN.

Seventy-one of the one hundred and eleven patients (64%) had immediate function of their grafts. Four patients (4%) had kidneys that never functioned and the rest (32%) recovered function after a variable period of dialysis (Table 3).

Twenty-eight percent (13/46) of the patients transplanted with kidneys perfused between 24-36 hours developed ATN. If the period of preservation was extended to 36-48 hours 63% (7/11) of the patients had ATN (Figure 4). Thus, there was a direct relationship of duration of preservation and the appearance of ATN after transplantation (Figure 5).

TABLE 2
Causes of Non-Function of Perfused and Transplanted Kidneys

Non-function	4 (3%)
Rejection	2
Technical	1
Preservation	1

TABLE 3
Outcome of Patients with Perfused and Transplanted Kidneys

Function of Perfused Kidneys (U of M only)	111 (100%)
Immediate	71 (64%)
Delayed*	36 (32%)
None	4 (4%)

*Required Dialysis.

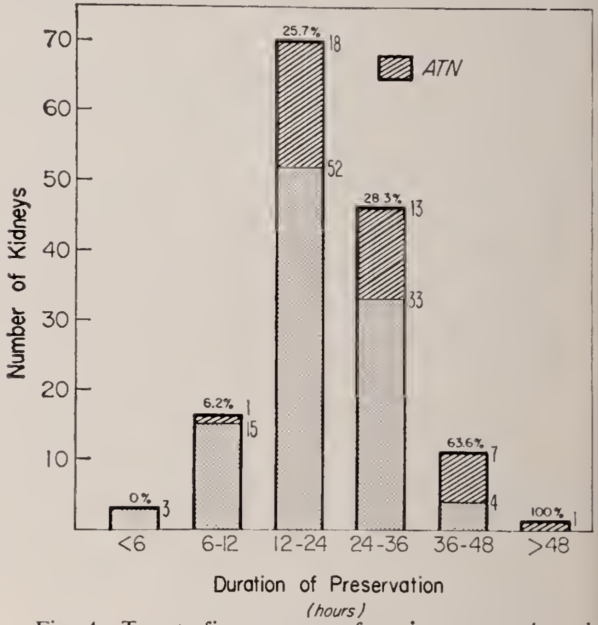

Fig. 4—Twenty-five percent of patients transplanted with kidneys that had 12-24 hrs. of preservation developed ATN. Longer periods of perfusion increased the presence of ATN.

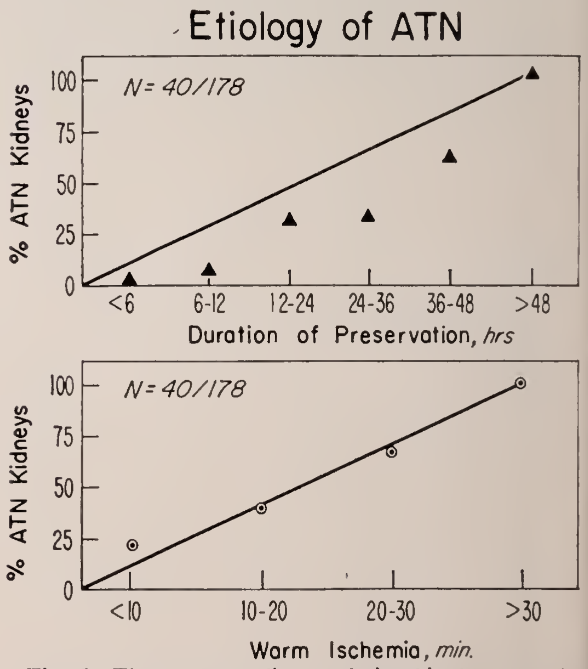

Fig. 5—There was a direct relationship between the duration of preservation and the presence of ATN. A similar relationship was observed in kidneys that underwent some period of warm ischemia before transplantation.

Warm ischemia as well as prolonged preservation had a similar effect upon transplanted kidneys (Figure 6). Forty percent (9/22) of the patients transplanted with kidneys that had 10-20 minutes of warm ischemia developed ATN. Longer periods of warm ischemia had a higher incidence of ATN. All kidneys (2/2) that had more than 30 minutes of warm ischemia developed ATN (Figures 7 and 8).

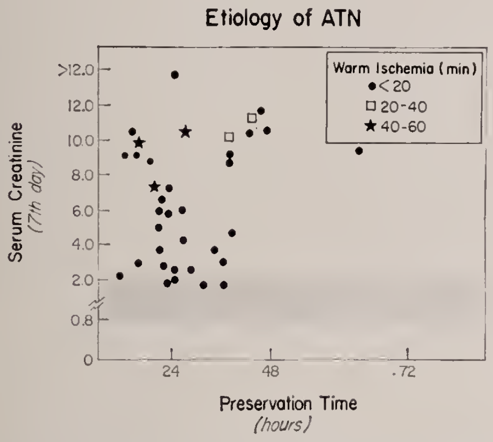

Fig. 6—Most of the kidneys that had some degree of warm ischemia underwent ATN changes. These kidneys also had a direct relationship to the duration of preservation.

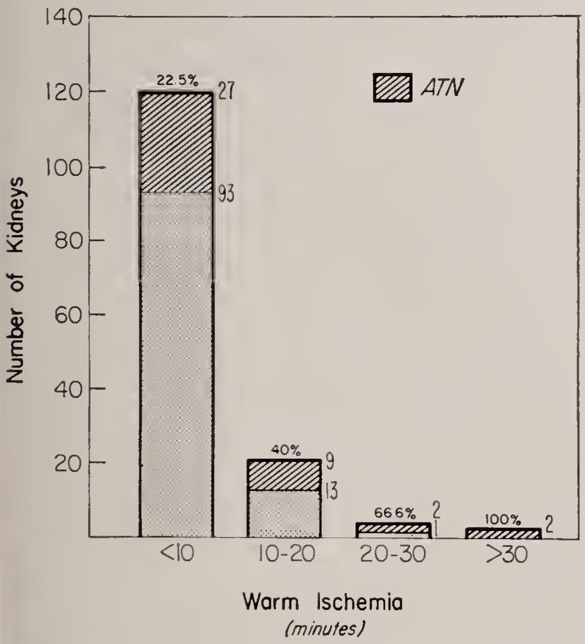

Fig. 7—There was a direct relationship between the warm ischemic damage and the presence of ATN. More than half of the patients who received kidneys that had more than 20 minutes of ischemic damage developed ATN.

Perfusate flow and systolic perfusate pressure were the most reliable indicators of viability during perfusion (Table 4). LDH, electrolytes, osmolarity or pH were not as reliable as flow and pressure.

During 1971 most of the cadaver donors (86%) were located at this University center. In the following two years they were equally located at other Institutions and Community Hospitals (Figure 9).

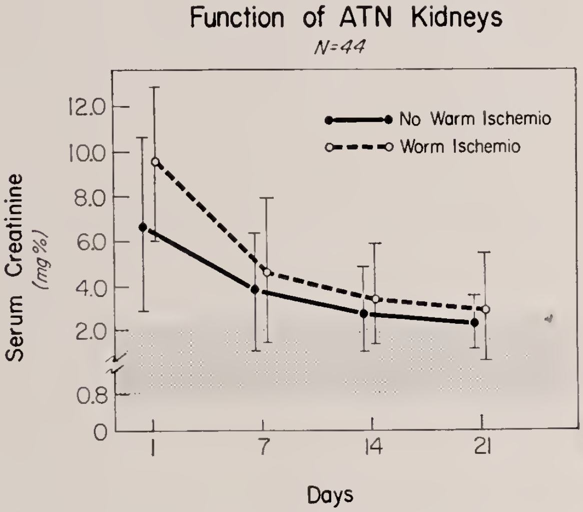

Fig. 8—There was a continuous and progressive recovery in the function of transplanted kidneys that developed ATN. The initial difference ($p < 0.01$) observed between warm ischemia and no warm ischemia kidneys was overcome at one week post-transplantation ($p > 0.5$). The kidneys which had recovered from ATN showed progress similar to those kidneys that did not develop ATN after transplantation.

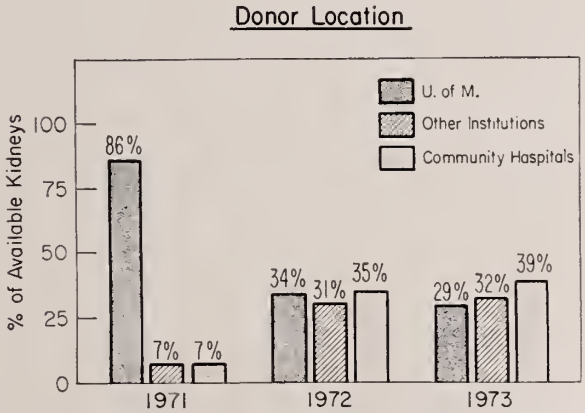

Fig. 9—Donor location changed in the last two years (1972-1973). Most of the donors were initially obtained from the University Center (1971), whereas in the last periods the Community and City Hospitals participated as well.

TABLE 4
Outcome of Kidneys with Increased Perfusate Pressure or Decreased Flow

Kidneys with ↑ Pressure	9 (6%)
Kidneys with ↓ Flow	19 (13%)
Discarded Kidneys	12 (8%)
Not Used	7 (5%)
Either ↑ Pressure or ↓ Flow with ATN	5 (3%)
Either changes with normal function	4 (3%)

With the modification and simplification of the organ preservation techniques, 68% of the kidneys were perfused while transported in 1972 and 1973. The rest of the kidneys were either transported in ice slush or combined ice slush and perfusion (Figure 10).

Discussion

Our experience with hypothermic pulsatile perfusion of cadaver kidneys demonstrates that this is an effective method for renal preservation. About two-thirds of the patients had immediate function after transplantation. Kidneys that did not work immediately after transplantation functioned in an average of one to two weeks. Only four kidneys (4%) never functioned after preservation and transplantation.

In cadaveric kidney allografts, warm ischemia (>20 min.) is the most important nonimmunological pretransplant event (preventable) that will determine the subsequent transplant renal function.[1,2,3,6] The presence of warm ischemia may imply (several) other factors affecting function: (1) poor preoperative donor preparation, (2) prolonged preoperative hypotension, (3) poor handling of the kidney during surgery, and (4) traumatic injury of the kidney. Furthermore, the duration of preservation influenced the outcome of the transplanted kidney. When preserved longer than 30 hours, most kidneys developed acute tubular necrosis. If kidneys were preserved no longer than 20 hours, however, no detrimental influence was made upon immediate subsequent function. From our data, it was apparent that both prolongation of perfusion and warm ischemia negatively influenced the *immediate* outcome of kidney function after transplantation from cadaver donors.

Hypoxia is probably the principal cause of damage of ischemic kidneys, and in the absence of oxygen the cell produces energy by glycolysis which is associated with lactic acidosis.[7] Without continuous and even perfusion severe suppression of aerobic metabolism occurs within minutes. During hypoxia the cell is forced to metabolize glucose with a minimal release of energy that eventually causes pump failure with the subsequent intracellular accumulation of sodium and water. The active extrusion of sodium at the cell membrane and the continuous shift of water determines cellular swelling that associated to metabolic acidosis accounts for high vascular resistance and poor perfusate flow during preservation.

Although phenoxybenzamine and methylprednisolone determined an improvement of perfusate flow and pressure with decreased vascular resistance in the clinically perfused kidney, they did not modify immediate posttransplant function. Other factors, such as rapid en bloc dissection and satisfactory maintenance of the fluid balance were essential to good kidney function.[8,9]

Long term preservation (>72 hours) by pulsatile perfusion is a different problem. The vascular endothelium is partially damaged and the perfused cell is susceptible to thrombotic processes or platelet aggregation after grafting. In addition, long periods of perfusion probably modify the mechanisms of water shifting with subsequent higher absorption of sodium. The response to this situation is the same, cellular edema that decreases perfusate flow and increases resistance. Methods designed to protect these kidneys are not available. Drugs used during preservation did not improve our results.

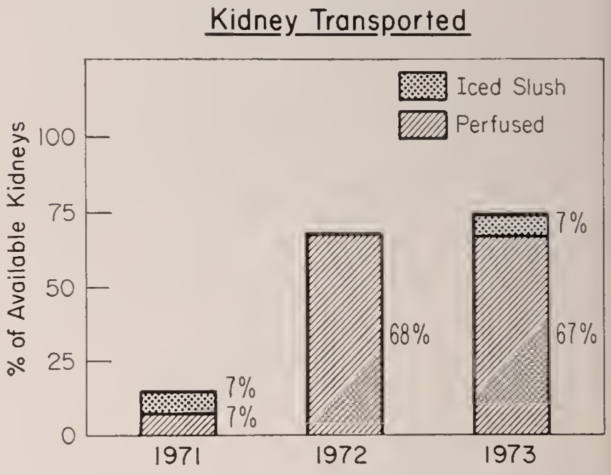

Fig. 10—The simplification of kidney preservation techniques allow us to perfuse most of the kidneys while being transported. A small number of kidneys were transported in iced slush only.

Prolonged preservation and ischemic damage are not the only problems in a cadaver procurement center. The inadequate supply of cadaver kidneys might represent the most pressing problem in any procurement program. It was evident from this study that the availability of donors and the source of these patients changed in the last two years. Most of the cases were concentrated at community or city hospitals. The establishment of a national organ procurement center could solve some of the problems created by poor donor availability. On the contrary, in some circumstances when several kidneys were obtained at the same time, it was difficult to find a suitable recipient.

It is of utmost importance to encourage a uniform preservation system of cadaver kidneys that would permit the more effective use of kidneys that otherwise would be eliminated because of potential technical problems. Most of the kidneys perfused under hypothermic pulsatile perfusion that had good flow and pressure functioned immediately upon implantation. Other viability tests were not as good as flow and pressure.

A real problem can be found in adequately perfused cadaver kidneys transplanted into recipients previously sensitized by prolonged hemodialysis. Even direct cross-matches of perfused kidneys performed with donor cell incubation with recipient's serum cannot avoid the presence of sensitization not detected by the present immunological techniques.[10] In addition, cytotoxic antibodies might be present in the cryoprecipitated plasma that would enhance the possibility of early malfunction posttransplantation.

The number of kidneys that were discarded is still high. A special effort should be directed to locate recipients, to avoid anatomical technical errors, and to protect kidneys that undergo prolonged warm ischemia.

The use of perfusion techniques for kidney preservation is advantageous in our experience, since several viability parameters, flow, pressure, pulsation, edema, etc., allow us to eliminate some organs that otherwise will undergo prolonged ATN after transplantation.

With the use of successful perfusion techniques and better kidney histocompatibility typing, there seems little reason why cadaveric transplantation should not be brought up to a level of success achieved at present with the living related transplants.

There are still two questions to be answered: the prolongation of renal preservation and the adequate treatment of ischemic kidneys. The clinical utilization of new perfusates with practically no lipids, higher concentrations of proteins, and increased osmolarity might improve the outcome of preserved kidneys. Furthermore, the protection of ischemic canine kidneys with allopurinol during preservation[11] gives a new potential application of this drug for clinical preservation.

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Resection of Rhabdomyosarcoma of the Neck

An Office Procedure

HARRISON H. FARLEY, M.D.*

THERE IS A REAL need for the practicing physician to conscientiously attempt to cut cost of his procedures for in this time of inflation the burden of even a few days hospital stay is just too much for the patient caught without adequate hospital insurance. Surgicenters have been springing up all over the nation, but do we really need them? No! Many of our more difficult procedures can be accomplished right in our offices. The following case in which a neck dissection was done as an office procedure using open drop ether anesthesia illustrates this point nicely.

A four-year-old male gradually developed over a few months' duration a swelling under his chin. This appeared initially to be in the midline but it grew to occupy not only the midline but both anterior cervical triangles. There seemed to be no encroachment upon the larynx or esophagus and the mass itself was of rubbery consistency.

The mass was for the most part ignored until it actually was larger than the poor fellow's head. There were no other palpable lesions or nodes on physical examination and he looked to be in good condition except for the huge neck mass. To cut cost we did no blood work and his chest Xray was eliminated.

The mass was movable and appeared to be free of attachment to any fixed structure. It seemed to me that this would be a good case to do in the office under open drop ether anesthesia.

On the 3rd of October, 1973, he was operated upon in the office treatment room. Mary Walters, R.N., who is not especially trained in anesthesia, administered the anesthetic and also assisted in the technical procedure. She was called upon to give artificial respiration on one occasion when inadvertently the patient slipped into Plane III of anesthesia. The patient came through this crisis nicely; in fact he roused to the point of actually making gurgling noises and struggling on the table during the tense period. One other problem that arose was that the surgeon got a bit giddy during one of the critical phases of the procedure when upon leaning too close he inhaled the vapors deeply and commenced to laugh inappropriately. However, this rather strange moment passed without harm to the patient.

We were able to nicely complete the dissection of the huge mass in its entirety and to get complete skin coverage of the resulting defect. The patient was placed in a makeshift bed and following office hours was discharged home with his family. Microscopic analysis of the specimen revealed it to be a highly malignant rhabdomyosarcoma. He came through the procedure beautifully, took nourishment that evening, and began to play about in his home the following day. He did well for over a month but unfortunately developed generalized metastases and succumbed approximately two months later.

This case illustrates that there is practically no limit to what can be done as an office procedure especially if the patient is a Hamster and willing to forego a few refinements normally found in the hospital setting. One must admit, however, that there is an increased element of danger involved in a case of this sort but on the other hand think of the money saved.

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*Minneapolis, Minnesota.

CME '76

May 20-21, 1976

Rochester, Minnesota

Special Article

Encroachment on the Private Practice of Medicine*

STUART V. THORSON, M.D.†

In recent years there has been a proliferation of programs to deliver "health care". These programs are delivering services we have always considered to be "medical practice." Four questions can be asked:

1. What forms are these programs taking?
2. Where do they gain their support?
3. Why are we vulnerable?
4. What can we do about these programs?

These questions will be discussed in order. "What forms are these programs taking?" How will we recognize them? We all know of the federal programs that are being promulgated for specific purposes. They include such as the programs on Maternal and Infant Care (MIC) and Early and Periodic Screening, Diagnosis and Treatment (EPSDT). These programs are targeted at limited populations and are subject to regulations and local interpretation for their implementation. These regulations and interpretations sometimes distort greatly the intent and purpose of the law. The EPSDT program in Minnesota has been interpreted by the State Department of Public Welfare as being primarily Early and Periodic Screening (EPS). This has resulted in the development of screening programs involving non-physicians such as nurse practitioners, public health nurses, and technicians who perform screening examinations and health assessment. The action by the State has in fact established an "alternative system of health care." Large numbers of allied health professions are being developed. The new allied health professionals include nurse practitioners, physicians' assistance, nurse clinicians and many others. They provide services as delegated by physicians but have aspirations toward independent practice and licensure.

A recent report from the Executive Director of the American Academy of Physicians' Assistants projected that 1500 graduates each year would be eligible to take the National Board of Medical Examiners certification examination. These programs are sponsored by the Council of Medical Education of the American Medical Association in collaboration with the American College of Surgeons, the American Academy of Pediatrics, the American Academy of Family Physicians and the American Society of Internal Medicine. Three-fourths of the graduates are in primary care settings and one-half of those work for general practitioners. Hospitals are developing and expanding programs to provide all levels of medical care. These programs include emergency rooms, satellite clinics, senior citizen's clinics and nursing services to senior citizen's housing, and are justified as meeting the needs of people which are not being met by the medical profession. Some hospital programs are being developed to provide a source of patients for empty hospital beds and others because their promoters feel they are more capable of organizing and directing medical services than are physicians. These programs usually require a licensed physician to be salaried by the hospital. All other services then are delivered by delegation through the use of that licensure and usually under the direction of someone other than that physician. Educational programs are being constantly expanded with more medical students, more graduate programs and consequently demands for a satisfactory volume of patients for clinical instruction. Institutions of learning are being required to provide primary medical services in order to obtain funding and certification even though those medical services fail to support the educational mission of medical training.

A health care delivery experiment in Boston utilizes paraprofessionals in first contact and in managing minor and common problems and requires algorithms or protocols to determine access to the physicians. This primary care is monitored by physicians using the computer.

"Where do these programs gain their support?" Support comes from legislators, politicians, health planners, from some physicians and from the people of the United States, the body politic.

"Why are we so vulnerable?" I submit that we are vulnerable because we have isolated ourselves from the body politic, we are not meeting the people where and as they perceive their needs. There has been a tendency to downgrade the importance of front line services, of listening and feeling for human needs. Several years back I saw a study of what nurses and social workers considered to be the role of the physician. To them he was a technician with special skills. Those questioned felt they should triage patients and prescribe the application of the technical skills of the doctor. Perhaps we have, as a profession, *abandoned those functions* which are now being *encroached upon by others.*

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* Presented before the House of Delegates on Saturday, November 15, 1975, Minneapolis.

† Family Practice Department, Hennepin County Medical Center, Minneapolis.

It is these allied health professionals who possess technical skills. Physicians should direct, delegate and supervise the use of such persons in clinical medicine. The abuse of this delegatory responsibility is the prime factor in this issue. That abuse is ours to police.

"What can we do about these programs?" Protest and attack on the behavior of others is not the answer. We must look to our own behavior. We must look to see if our performance measures up to the needs of the people. As indicated by the Millis Report we have been for too long emphasizing the knowledge and skills of medicine while paying little if any attention to our attitudes. Knowledge and skills define technicians. Attitudes give purpose and direction to knowledge and skills. Medicine is a noble and serving profession. It must address people and their needs. We needn't go to the "barefoot doctor program" to gain humility but perhaps we should reflect on what being a doctor requires of each one of us. Let us look to the heritage of our profession, to its philosophy, and then blend our technical skills with the attitudes required to be a complete physician. Then our behavior will reflect our ability to function as doctors and be what we must be. We cannot rest upon our knowledge which is vast and our technical skill which is superb and expect to continue to merit the confidence of the people of this country. We must develop attitudes which assure the body politic that physicians can be trusted to do what is right and proper. *To be a physician is to be available. To be a physician is to listen. To be a physician is to serve. To be a physician is to be competent, to have the knowledge and skills that are appropriate to the needs that are expressed by our patients.* It is the primary physician who has accepted the responsibility on behalf of his profession and the people he serves to be "our doctor". This goal requires an attitude of function and an acceptance of responsibility that must be nurtured by the whole profession. It is that role which gives direction and purpose to what we are about. *Being a doctor first* must be the prime allegiance of each one of us.

Accreditation of Programs in Continuing Medical Education

The Minnesota State Medical Association has begun the process of accrediting Minnesota hospitals and other organizations sponsoring programs in Continuing Medical Education for physicians. It is the intent of the MSMA to accredit the sponsoring organizations for all of their ongoing CME activities and not the individual courses and programs. As the system of accreditation becomes fully operational, all hospitals and medical specialty societies in the state will be notified how to apply. Meanwhile, your questions should be directed to Paul F. Bowlin, M.D., Chairman, Accreditation Subcommittee, in care of the MSMA office.

Inquiries concerning any other aspect of the CME program may be directed to the MSMA office in care of Dr. John S. Welch, Chairman of the Medical Education Committee.

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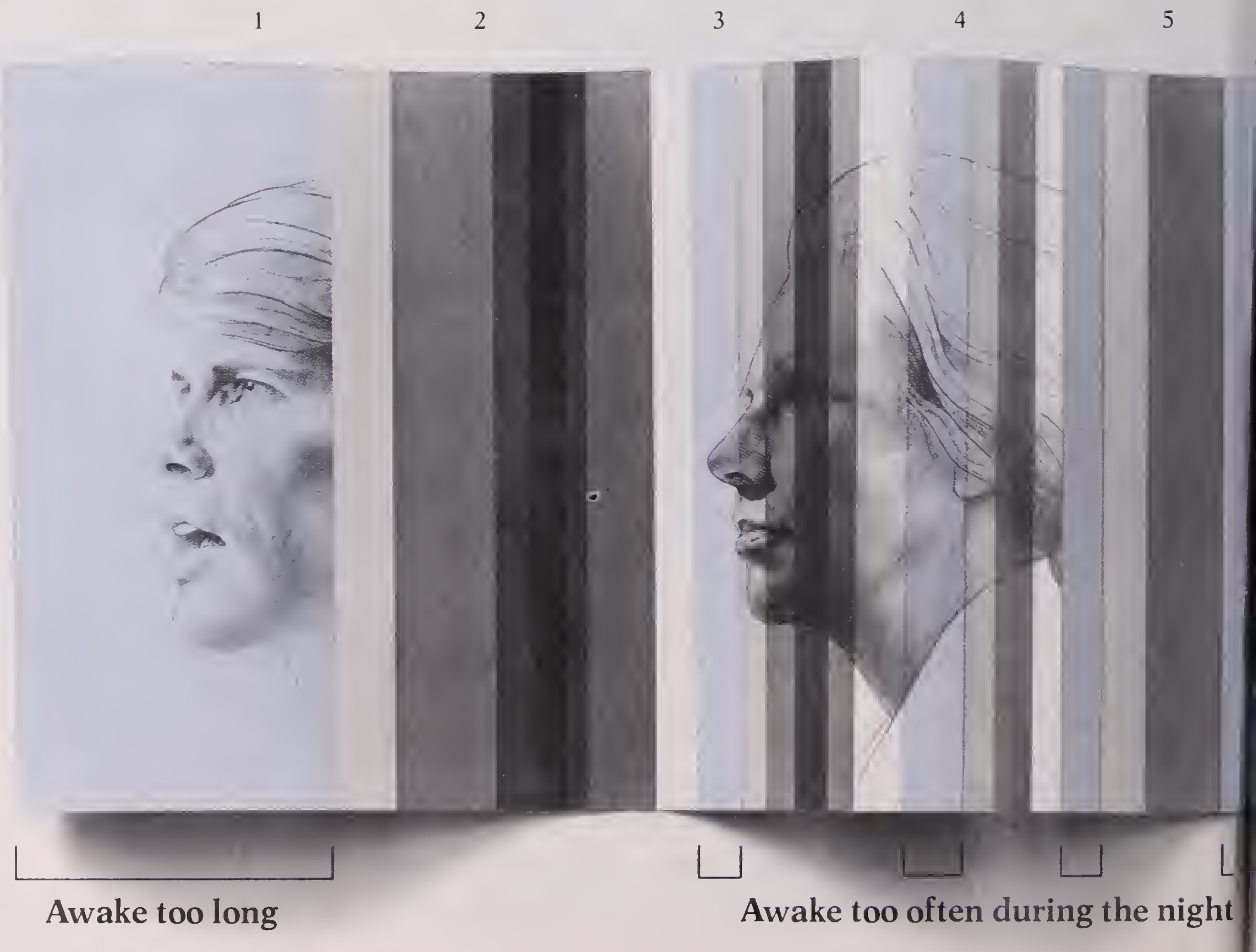
Sleep Stages

□	Awake	■	Stage 2
□	REM	■	Stage 3
□	Stage 1	■	Stage 4



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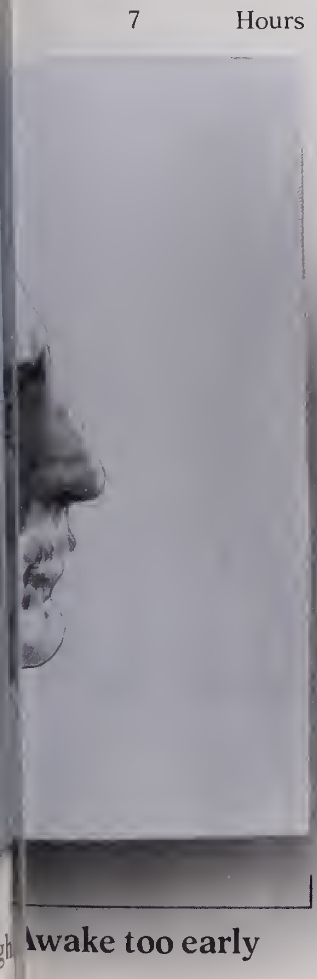

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Please see following page for a summary of complete product information.

Broad-spectrum medication for the most common forms of insomnia

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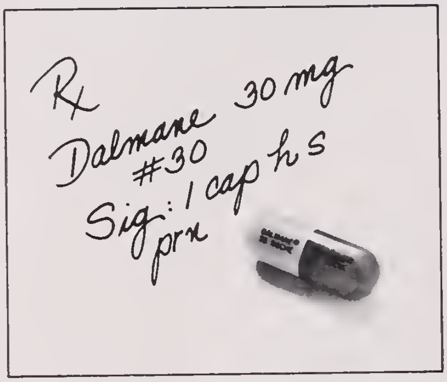
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Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

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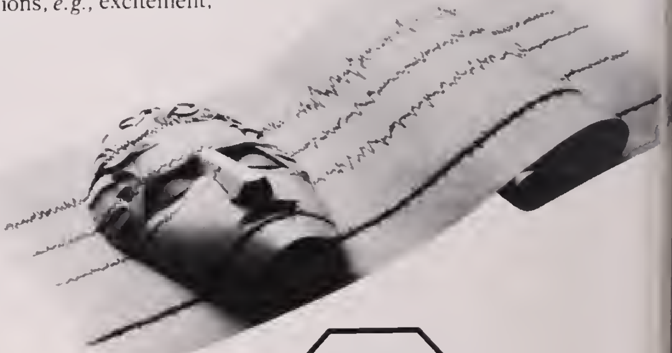
3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ



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Editorials

Clinical Effects of Warm Ischemia and Prolonged Preservation on the Outcome of Transplanted Kidneys

In this issue Dr. Toledo-Pereyra and his associates* have again directed attention of surgeons involved in clinical renal transplantation to the detrimental effect of prolonged warm ischemia time and prolonged preservation especially with reference to the occurrence of acute tubular necrosis.

Timely and technically competent organ procurement of the diuresing kidney is of utmost importance. In addition, use of vasoactive and membrane stabilizing drugs in pretreating donors has been demonstrated to be beneficial in preventing ischemic damage to the renal graft. Prolonged preservation, though occasionally necessary, or the perfusate per se may harm the allograft. At the Mayo Clinic pulsatile perfusion under hypothermia with cryoprecipitated plasma similar to the one used by the authors is still performed. It is our current policy to perform crossmatches between the perfusate and the donor lymphocytes to detect cytotoxic antibodies in the perfusate. If feasible, pulsatile perfusion is avoided entirely, and the kidney after initial flush and short storage in slush is transplanted as early as possible in the already prepared recipient. This of course is not always possible, especially when the kidneys are to be transported. Since early transplantation in combination with pretreatment of the donor with vasoactive agents and high doses of cytotoxic drugs and methylprednisolone has been employed, a significant increase in survival of our cadaveric renal allografts has been noted (over the last two years). In addition, no instance of acute tubular necrosis necessitating hemodialysis has been observed in the last 40 cadaveric renal allografts procured and transplanted in our own center.

Horst Zincke, M.D.†
Rochester, Minnesota

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*See page 18.

†Transplantation Surgery, Mayo Clinic.

Functional Dermatochalasia

Doctor Carroll's excellent article, "Functional Dermatochalasia,"* appropriately emphasizes important features in the evaluation of the patient with involutional changes in eyelid tissues. Most importantly, he has reminded us that careful attention to the ocular symptoms of patients who are being considered for upper lid blepharoplasty may reveal associated disorders that are amenable to surgical therapy for functional, not cosmetic, reasons.

Certainly, visual field impairment, especially in the upper temporal fields, can result from excessive redundant upper eyelid skin, the removal of which will alleviate the visual field defect. However, such patients should be evaluated for drooping of the eyebrows; and if we follow Doctor Carroll's suggestion that careful attention be paid to eyebrow position and symptoms suggesting sustained frontalis muscle activity, the patient may be much happier postoperatively if surgical therapy is directed toward elevating the eyebrows as well as

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See page 15.

conventional blepharoplasty. When blepharoplasty is combined with lifting of the eyebrows, this usually means that less redundant eyelid skin will have to be removed.

Doctor Carroll has mentioned that many patients requesting blepharoplasty will have accompanying involutional ptosis, which can be repaired at the time of blepharoplasty (usually by tarsomyectomy). Conversely, some patients with upper lid retraction usually secondary to Graves' disease may be requesting blepharoplasty when, in fact, the elevated eyelid is the problem, and the excessive eyelid skin is more apparent than real. In these patients, therapy should be directed toward relief of the eyelid retraction, the correction of which not infrequently may make blepharoplasty unnecessary or lessen the amount of redundant skin to be excised.

Doctor Carroll wisely suggests that the patient show the physician in the mirror precisely what it is about the appearance of the eyelids that is bothersome. This also provides the physician with the opportunity to discuss what might be achieved by surgical intervention. Such an exercise can avoid disappointment postoperatively on the part of both patient and surgeon.

Fat removal in the upper lids in conjunction with blepharoplasty deserves special mention. The medial fat pad is more often responsible for cosmetic liability than the temporal fat pad and can usually be removed with safety. As a rule, this fat pad is smaller and less yellow in color than the temporal fat pad and is located medial to the levator aponeurosis. On the other hand, removal of the temporal, or preaponeurotic, fat pad is risky and should with extreme caution be performed because of: (1) the danger of injuring the levator aponeurosis; (2) the possibility of creating adhesions between the orbital septum and the aponeurosis, resulting in a higher or asymmetric lid fold; and (3) the possibility of creating a deep supratarsal sulcus, which may be highly undesirable, especially in patients of oriental ancestry, who do not wish to alter the appearance of their upper eyelids in this manner.

Meticulous hemostasis and removal of only that amount of fat that will prolapse easily are essential because postoperative hematoma can cause a serious cosmetic problem and vigorous manipulation of orbital fat may well be related to the devastating complication of blindness that has been reported on several occasions after blepharoplasty.

This is a fine article and well worth critical analysis by those who perform ophthalmic plastic surgery.

Robert R. Waller, M.D.*
Rochester, Minnesota

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*Mayo Clinic and Mayo Foundation.

Shotwell Award
Metropolitan Medical Center

Doctors Frank E. Johnson, Joseph C. Kiser, and Theodore A. Peterson were presented the Shotwell Award by the Metropolitan Medical Center for their humanitarian work on behalf of heart crippled children from around the world.

The Shotwell Award was established in 1971 in honor of Mr. and Mrs. James D. Shotwell for their financial contribution to MMC and is presented annually for noteworthy effort in the field of health care in one of the following categories: (1) dedicated service to mankind, (2) breakthrough in research or other major contribution to the field of medicine and (3) innovation or improvements in health care delivery, including health care legislation.

Letter to the Editor

Inflation and Medicine 1954 - 1974

Dear Editor:

A great deal of dialogue has been directed toward the increase in the cost of medical care over the past 20 years and as a *generality* the basic premise is true.

In evaluating this increase in the cost of medical care, several factors must be considered. First, "medical care" must be subdivided into actual physician costs and non-physician costs such as hospital care, custodial care, drug costs and other non-physician care costs. Second, and equally important, we must consider that the average person—with increased insurance coverage, purchasing power and welfare—requires or demands more care than 20 years ago. In other words, while the cost of the same medical care has increased, there has been an equally significant increase in the amount of medical care.

In connection with this question, we did some random sampling of figures on inflation, physician fees and physician income for the 20-year period 1954 to 1974. Statisticians would very probably regard these figures as superficial and perhaps inconclusive, but they do give us a "bird's-eye view" of what has happened over this 20-year period.

Inflation—as measured by the Consumer Price Index, U.S. Department of Labor:

From 1954-1959	Average Annual Inflation	2.0%
From 1959-1964	Average Annual Inflation	1.3%
From 1964-1969	Average Annual Inflation	4.2%
From 1969-1974	Average Annual Inflation	6.7%

1973 Rate 6.2%
1974 Rate 11.0%

Using a base of 100% for 1954, the Consumer Price Index would have been 110% for 1959, 119% for 1964, 145% for 1969 and 203% for 1974. This index has risen 103% in 20 years, with a 45% increase the first 15 years and 58% the last 5 years.

In attempting to relate this rate of inflation to physician medical care, we sampled fees in nine medical specialties and found that these fees have gone up an average of 74%, with individual increases ranging from 133% for some office calls down to a low of 47% for refractions by Ophthalmologists. It appears that physicians' professional fees in the areas that we service have gone up about 29% less than the Consumer Price Index.

Next, we sampled net professional income for physicians in these same nine specialties and found that net income had risen from an average for all nine specialties of $30,400 in 1954 to an average of $71,200 for 1974, an increase of 134%. This is 31% higher than the Consumer Price Index rise.

However, we immediately concluded that if average fees have increased 74% and profits have increased 134%, that increased productivity has to account for the remaining 60% increase in profit. Considering the 74% increase in fees on the increased productivity indicates that our average client in these nine specialties is actually achieving about 35% more physical production than in 1954.

Then comes the "great equalizer"—Federal and State Income Taxes. On the average income of the nine specialties in 1954 of $30,400, the Federal and State tax burden would have been about $7,400, leaving $23,000 spendable income. In 1974, on a $71,200 income, the tax burden would have been about $24,700, leaving $46,500 spendable income. This is an increase in spendable income of 102% or 1% less than the rise in the Consumer Price Index.

Our conclusion from this brief study is that physician fees for these nine specialties rose 29% less than the price index, these doctors generated 35% more production, realized net income 31% higher than the price index—all this for the final result of having 1% *less* spendable income than in 1954.

Obviously, there are variations from one of the nine specialties to another, resulting in some practices benefiting and some being penalized by inflation, but generally speaking, there is no indication that physicians have contributed more than their share to inflation: On the contrary, we must conclude that our average client is producing about 35% more to not-quite keep pace with inflation as it affects his own spendable income.

Howard D. Baker*
Waterloo, Iowa

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*Professional Management Midwest, 621 Grant Avenue, Waterloo, Iowa.

Philosophical Musings of a Surgeon

Heroics in Medicine

"Something *must* be done, Doctor. Don't spare expense. Just *do* something." These are the familiar and desperate adjurations of family and relatives, who during the terminal illness of a "loved one," may instigate the physician to exceed his better judgment.

Heroics in medicine and surgery is a commendable procedure when there are sufficiently sound and convincing reasons to pursue it; but to submit a patient to the hazards, miseries, morbidities, and expense of essentially futile efforts is no more commendable than its opposite practice: the ancient Eskimos' custom of retiring their fatally ill and useless aged to the expeditious mercies of an ice floe.

Life-threatening diseases and injuries, with a subordinate chance for useful recovery, should be so treated as to minimize morbidity. Heroic measures are justifiable only when the odds for useful recovery are predominant even though the risks are high.

A ninety-year-old physically active and mentally alert patient with a recent cataract is a good candidate for surgery; but a similar patient with an incurable carcinoma should not be burdened with the numerous morbidities that might develop in an attempt to prolong life for a few more months.

A patient with a neck-and-back strain from a rear-end collision is eligible for a routine physical examination, appropriate x-rays and a few days of physio-therapy; but a costly, time-consuming, extensive battery of sophisticated tests and examinations, under a platoon of specialists, each for his own narrow field of interest, would seem to be redundant.

In this vein I could continue—ad infinitum.

Not only in such fields as economics, but also in medicine is the principle of cost-benefit-ratio applicable and operative, keeping in mind that while the benefits may be only marginal at best, the costs may be excessive in terms of physical, emotional, and even mental trauma and anguish. In short, are the benefits worth the costs?

Lest we be justifiably faulted in our enthusiasm and dedication to saving lives and restoring health, let's again and again evaluate our efforts and immediately classify them: as unnecessary, elective, urgent, emergent, heroic—each category with its own spectrum of gradations.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus

X-Ray Conference

Diarrhea in a Patient with Renal Failure

A 60-YEAR-OLD MAN was admitted to Hennepin County Medical Center on July 3, 1975 for treatment of acute renal failure of unknown cause.

In 1971 the patient had a laminectomy plus spinal fusion for lumbar disc herniation. In May, 1975, he was again operated on for adhesive arachnoiditis and cauda equina compression. Staphylococcal infection of the wound ensued, and cleared only after the administration of various antibiotics over several weeks. The antibiotics used included lincomycin, chloramphenical and dicloxacillin. On June 27 he developed headaches, nausea, vomiting, fever and chills. All bacteriological studies were negative. Keflin therapy, 2 gm. I.V., every six hours, was started on June 28. The BUN was 29 mg.% in May, 1975, 55.5 mg.% on June 29 and 110 mg.% on July 2. Because of the rising BUN, the patient was transferred to the Medical Center.

The positive physical findings were mild confusion, lethargy, and abdominal distention with decreased bowel sounds. The temperature, pulse, respiration, and blood pressure were normal. The white count was 7,700/cmm., PMN 90%, lymphocytes 10%, Hgb 12.1 gm.%. Serum sodium 123 mEq., potassium 5.2 mEq., chloride 82 mEq., and CO_2 15 mEq./liter. Blood sugar 59 mg.%. BUN 115 mg.%. The chest radiograph was essentially normal. The FCG disclosed nonspecific ST-T changes.

The patient was started on hemodialysis. On July 5, he began to pass guiac-positive stools. This was followed by frank diarrhea with passage of blood and mucus. A barium enema examination of the colon was performed on July 11 (Figures 1, 2). (What is your diagnosis?).

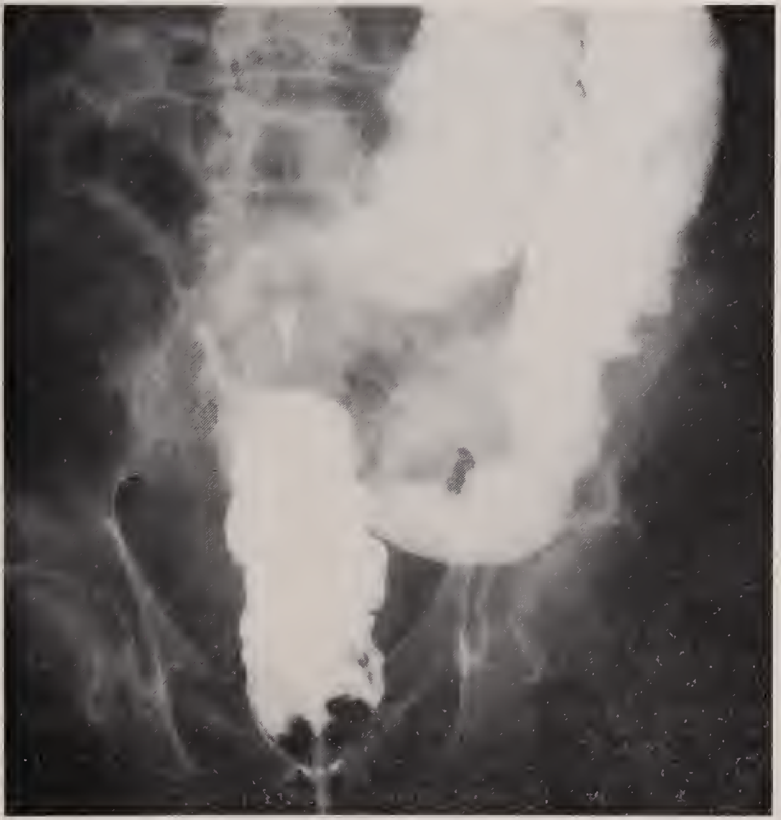

Fig. 1—Barium-filled lower colon showing shaggy, edematous mucosa. Ulcers and small polypoid filling defects are present but not well seen. There is residual myelographic medium in the sacral canal.

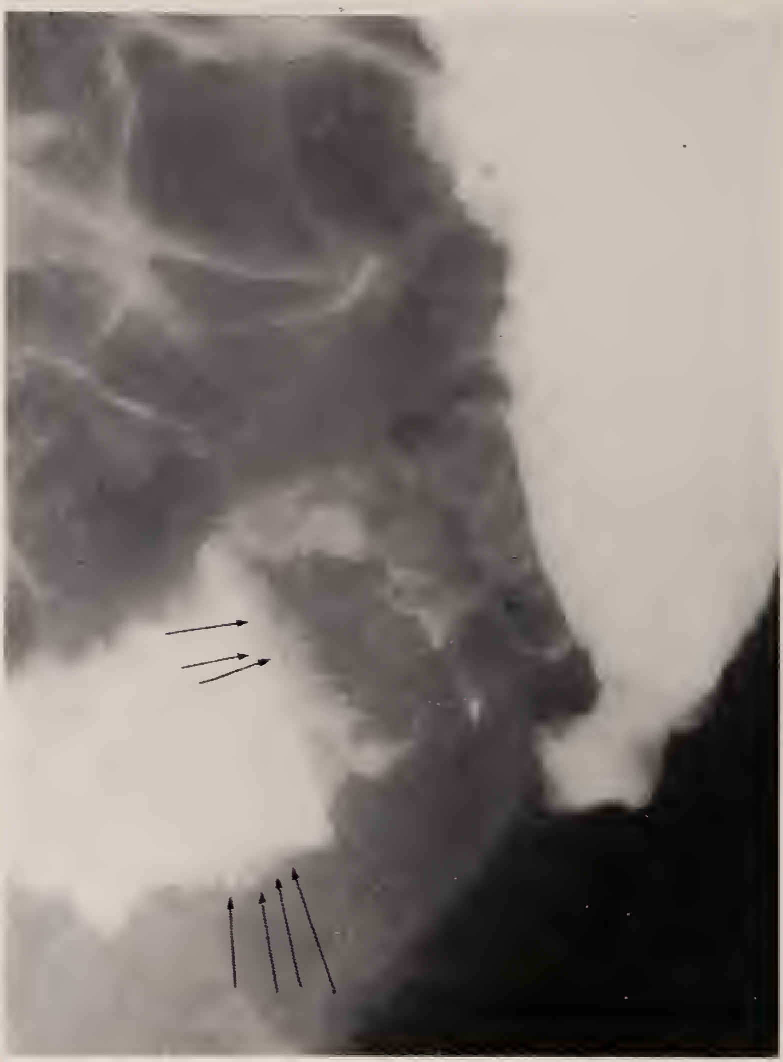

Fig. 2—Spot films of the sigmoid colon disclosing small ulcers (lower arrows) and polypoid filling defects (upper arrows). The defects are caused by the small plaques on the colonic mucosa.

Diagnosis: Pseudomembranous Enterocolitis

The barium filled colon was shaggy in appearance (Figure 1). Its walls showed serrations caused by ulcers (Figure 2). Numerous small round filling defects (Figure 2) were also observed. Sigmoidoscopy on the same day revealed edematous and friable mucosa studded with numerous, 3-4 mm. whitish plaques. Stool cultures grew normal flora.

The diarrhea subsided under supportive treatment. Sigmoidoscopy was repeated on July 9, and disclosed a nearly normal mucosa with slight granularity. On August 21 the barium enema demonstrated a normal colon.

Discussion

Pseudomembranous enterocolitis, a serious disease, has been known since 1867, when Billroth made the first report. It has been associated with surgical procedures, debilitating diseases (such as lymphoma and leukemia), bowel obstruction, hypotension, uremia, staphylococcal overgrowth, and antibiotic therapy. Among the antibiotics incriminated are penicillin, tetracycline, chloramphenical, ampicillin, lincomycin, and clindamycin. Many reports of clindamycin-related cases, some fatal, have appeared in the recent literature. In our patient, either the uremia or one or more of the antibiotics used could have been the offender.

Grossly the involved bowel mucosa is reddened, edematous, friable, and showed many small, whitish plaques on its surface. Microscopically the plaques are pseudomembranes consisting of fibrin, mucus, inflammatory cells and cellular debris. Ulcers are left behind when they slough off. The goblet cells are distended with mucus. The lamina propria has leukocytic infiltration. The submucosa is edematous. The radiographic picture correlates well with the pathological features.

In the presence of the appropriate clinical setting, the onset of diarrhea should alert one to the possibility of pseudomembranous enterocolitis. Proctosigmoidoscopy is the most definitive diagnostic procedure. The barium enema examination is also of high diagnostic value, and reveals the extent of the bowel involvement. Because of the radiographic findings of ulceration and polypoid filling defects, ulcerative colitis is almost always considered in the differential diagnosis. "Thumb-printing" due to mucosal edema may be seen occasionally, and may cause confusion with ischemic colitis.

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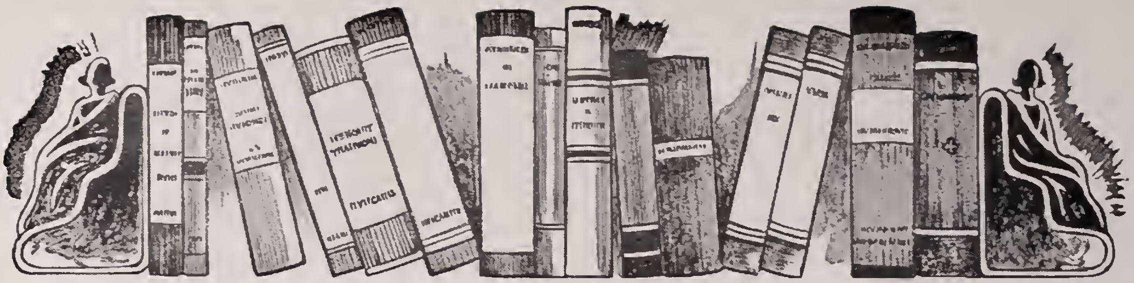
Cover Photo

"Journey's End"

Dr. Don Carlon's sculpture is featured on this month's cover. It is constructed of bronze and copper and was commissioned by the City of Fargo, North Dakota, and presented to the people of Norway. It is now housed in the Storting (Parliament Building) in Oslo, Norway and was to commemorate the 150th anniversary of the Norwegian immigration to this area.

Dr Carlon tells the editors that this vehicle was the only mode of transportation for the immigrants in the 1800s. It depicts the prairie schooner or Conestoga wagon.

Another of Dr. Carlon's sculptures appeared on the May, 1975 cover of Minnesota Medicine. Dr. Carlon is a practicing radiologist in Moorhead.



Book Reviews

BONE MARROW MORPHOLOGY AND MECHANICS OF BIOPSY. By Emil Maro Schleicher, 193 pp, 165 illus, $16.75, Charles C. Thomas, 1973.

In the past 35 years Doctor Schleicher has aspirated bone marrow from the sternums of 15,000 patients. Also he has written 70 papers on this experience and has contributed original observations about bone marrow, including the presence of lymphatics, hematoxylin bodies in lupus, Hodgkin's cells, mononucleosis nodules and metastatic carcinoid.

In addition, Dr. Schleicher has designed marrow biopsy instruments. He writes extensively about each in his book. The instruments include an aspiration and tissue core unit. The aspiration instrument allows him to safely and quickly withdraw 5 to 10 ml marrow. He then concentrates the marrow, smears the buffy coat and serially sections "gross-marrow units," the basic structural and physiological components of the marrow organ.

Why 5 to 10 ml of marrow? After all, most hematologists recommend only a drop or two or a few milliliters at most. Because Doctor Schleicher conceives of the marrow as an organ. To examine it completely, he feels you need an adequate sample. Only then can you look at its basic pattern and exclude granulomas, metastases, and other disease.

According to Dr. Schleicher "Marrow Units" vary in volume, size, shape and pattern, depending on the underlying disorder. Disease begins in the units, and all marrow cells evolve out of toti-potential reticulum cells.

These units, the reticulum cells, and their interrelationships form the basis of Doctor Schleicher's concept of the marrow organ. ,

After reading the book, another of his beliefs looms clear: his ideas aren't worth much unless the "hematopathologist" pays scrupulous attention to technical details—from preparing the patient, to aspirating the sample, to staining, to serially sectioning marrow units, and to allowing for color blindness. Because of this belief, the book has many highly technical sections. These are, frankly, heavy going. But also because of this belief, his photomicrographs, especially ones in the color atlas of marrow biopsies, are sharp, clear, and appropriate.

Richard L. Reece, M.D.
Editor-in-Chief

ABDOMINAL OPERATIONS, Volumes 1 and 2, Sixth Edition. Rodney Maingot. Appleton-Century-Crofts/New York 1974. Pages 2240. Price: $82.50.

Maingot has produced a prodigious two-volume book on Abdominal Operations, recognizing, no doubt, the enormous new material in the field of abdominal surgery, as well as the procedures that have remained standard for many years.

For the young surgeon who is given the responsibility of setting up his profession in a rural area where new and modern hospital facilities make it possible for him to practice good surgery, these volumes should be immediately available to him in order that he .can have the opportunity to review any problem of abdominal surgery that confronts him.

Etiologic factors and diagnostic differentiation are briefly, but adequately, included.

The wash drawings and pen-line sketches are an asset to the written descriptions of surgical technique and need no greater detail for the surgeon who has been adequately trained.

References are included at the end of each chapter.

Volume One deals with the upper gastrointestinal tract: stomach and duodenal, spleen, pancreas and the gallbladder system. Volume Two includes the liver, the intestinal tract, and a few special subjects—all pertaining to abdominal problems.

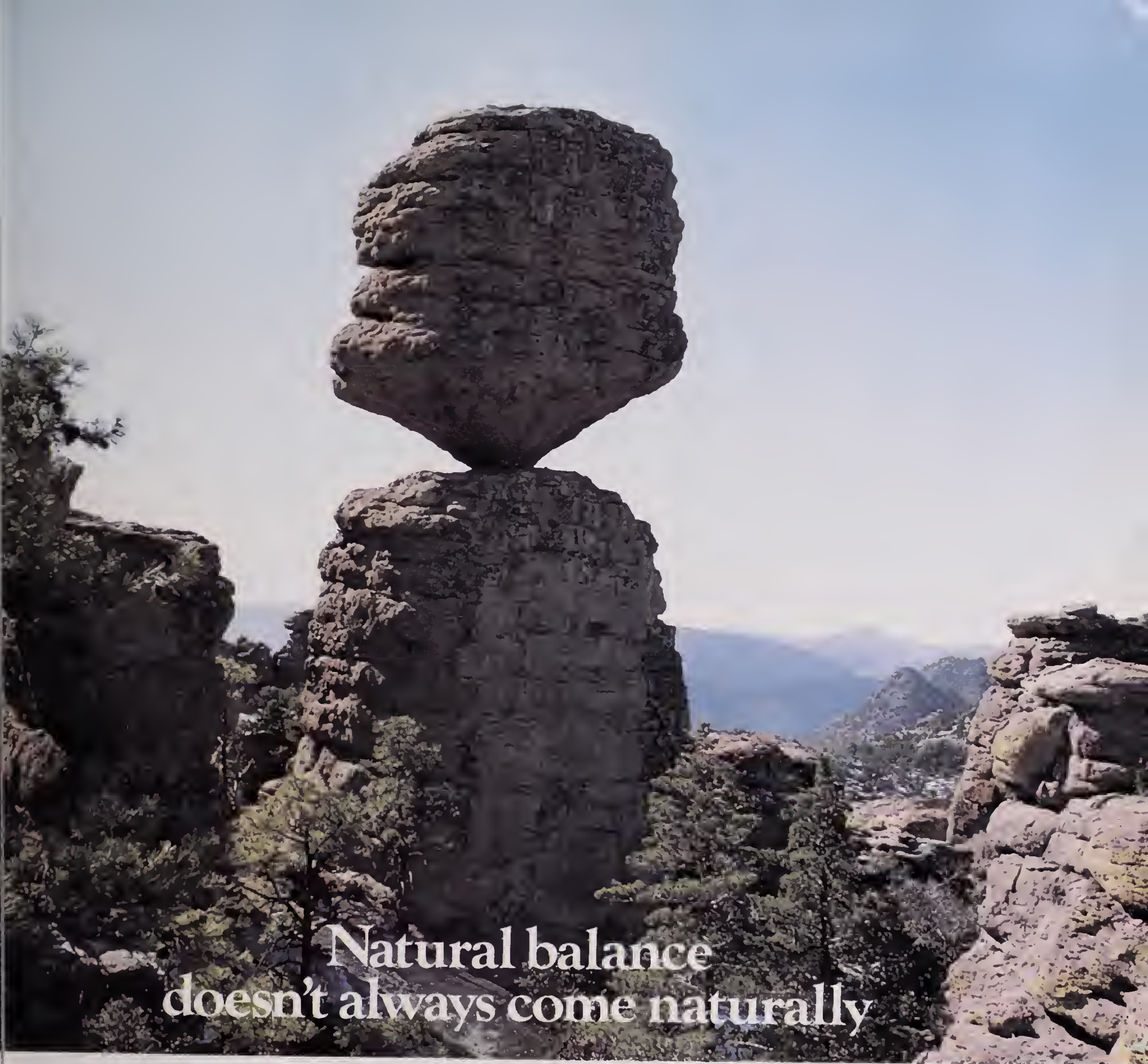
All young surgeons would be well rewarded to have this book; established surgeons would enjoy it for its excellence.

Carl O. Rice. M.D., Ph.D.
Editor Emeritus

YOUR PERSONAL LEARNING PLAN, A HANDBOOK FOR PHYSICIANS by Leonard S. Stein, Ph.D., Copyright 1973 by the Illinois Council on Continuing Medical Education, 360 North Michigan Avenue, Chicago, Illinois 60601, 32 pages, $1.00.

This handbook is generally for the active practitioner who wishes to pursue postgraduate studies in a systematic manner. The handbook divides the approach to the learning process into seven successive steps. Work sheets are provided to inventory specific needs, to establish priorities and to initiate a program of learning. The learning opportunities section is a most valuable resource. In general it lists some of the opportunities available throughout the United States. Most importantly, it underlines the necessity to be critical in evaluating courses and learning material. With the increased emphasis in recent years on self-evaluation and continuing medical education by such groups as the American Academy of Family Practice, the American College of Surgeons and the Minnesota State Medical Association, this handbook comes at an opportune time.

S. F. Ceplecha, M.D.
Redwood Falls, Minnesota



Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

und useful in the management of vertigo* associated with ses affecting the vestibular system.

relieve nausea and vomiting often associated with vertigo.*

ual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.

o available as Antivert (meclizine HCl) 12.5 mg. scored s, for dosage convenience and flexibility.

tivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for a, vomiting and dizziness associated with motion sickness.

UMMARY OF PRESCRIBING INFORMATION

ICATIONS. Based on a review of this drug by the National Academy of ces—National Research Council and/or other information, FDA has classified dications as follows:

ctive: Management of nausea and vomiting and dizziness associated with n sickness.

sibly Effective: Management of vertigo associated with diseases affecting the ular system.

al classification of the less than effective indications requires further igation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy. See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG *Pfizer*
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert®/25
(meclizine HCl) 25 mg. Tablets
for vertigo*

Documented bioavailability...
Regimen flexibility
q.i.d. or q 6h immediately after or between meals

E-Mycin®
erythromycin enteric-coated tablets, Upjohn
250 mg
Formulated for quality...
Priced for economy.

Upjohn

See facing page for brief summary of prescribing information.

J-4889-9

-MYCIN® TABLETS — 250 mg — For Oral Administration (eryhromycin enteric-coated tablets, Upjohn)

-Mycin Tablets (erythromycin enteric-coated tablets) are speially coated to protect the contents from the inactivating effects f gastric acidity and to permit efficient absorption when adinistered either immediately after meals or when given beveen meals on an empty stomach.

ndications: *Streptococcus pyogenes (group A beta-hemolytic reptococci):* Upper and lower respiratory-tract, skin, and softssue infections of mild to moderate severity. Parenteral benzaine penicillin G is considered by the American Heart Associaon to be the drug of choice in the treatment and prevention streptococcal pharyngitis and in long-term prophylaxis of eumatic fever. When oral medication is necessary (because e parenteral route is contraindicated) or if there is known lergy to penicillin, the following recommendations made by e American Heart Association apply: 1) Oral penicillin G or V here no allergy exists)—This is the drug of choice. Give for minimum of 10 days; 2) Erythromycin—Give for a minimum 10 days. A few strains of streptococci resistant to erythroycin have been reported.

oha-hemolytic streptococci (virdans group): Short-term proylaxis against bacterial endocarditis prior to dental or other erative procedures in patients with a history of rheumatic ver or congenital heart disease who are hypersensitive to nicillin. (Erythromycin is not suitable prior to genitourinary rgery where the organisms likely to lead to bacteremia are am-negative bacilli or the enterococcus group of streptococci.)

aphylococcus aureus: Acute infections of skin and soft tissue mild to moderate severity. Resistance may develop during atment.

plococcus pneumoniae: Upper respiratory-tract infections g., otitis media, pharyngitis) and lower respiratory-tract intions (e.g., pneumonia) of mild to moderate degree.

coplasma pneumoniae (Eaton agent, PPLO): In the treatment primary atypical pneumonia, when due to this organism.

ponema pallidum: Infections due to this organism.

Corynebacterium diphtheriae and *Corynebacterium minutissimum:* As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers. In the treatment of erythrasma.

Entamoeba histolytica: In the treatment of intestinal amebiasis only. Extra-enteric amebiasis requires treatment with other agents.

Listeria monocytogenes: Infections due to this organism.

Contraindication: Contraindicated in patients with known hypersensitivity to erythromycin.

Warning: Safety for use in pregnancy has not been established.

Precautions: Erythromycin is principally excreted by the liver. Caution should be exercised in administering the antibiotic to patients with impaired hepatic function. Surgical procedures should be performed when indicated.

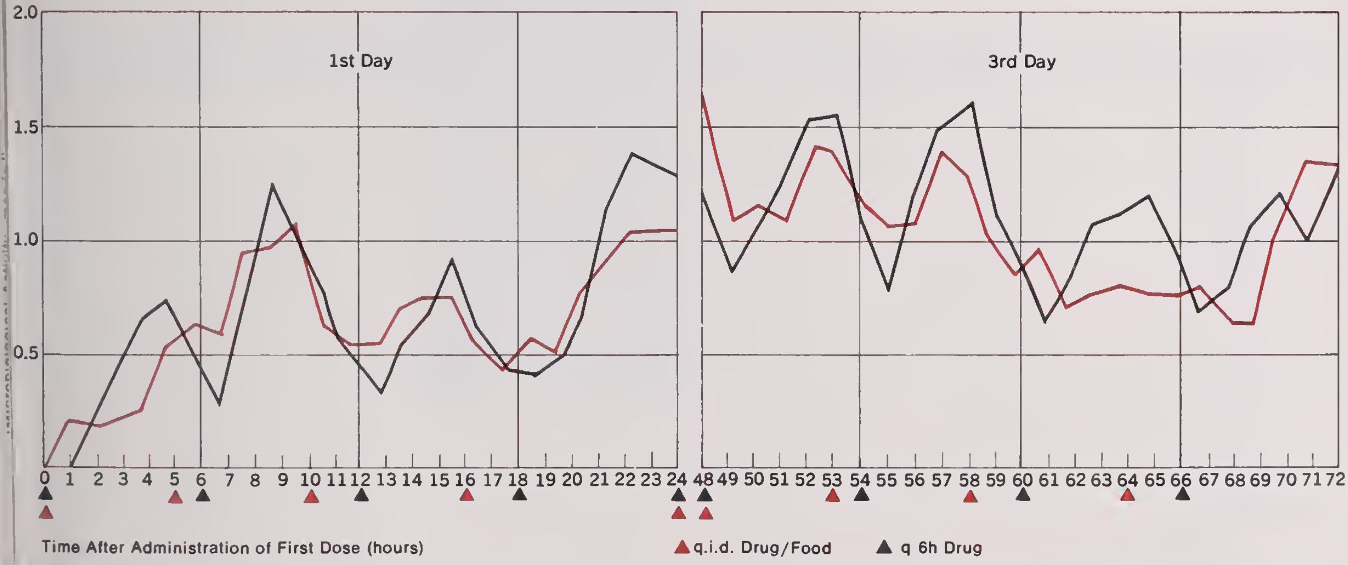
Adverse reactions: The most frequent side effects of erythromycin preparations are gastrointestinal, such as abdominal cramping and discomfort, and are dose-related. Nausea, vomiting, and diarrhea occur infrequently with usual oral doses. During prolonged or repeated therapy, there is a possibility of overgrowth of non-susceptible bacteria or fungi. If such infections occur, the drug should be discontinued and appropriate therapy instituted. Mild allergic reactions such as urticaria and other skin rashes have occurred. Serious allergic reactions, including anaphylaxis, have been reported.

Treatment of overdosage: The drug is virtually nontoxic, though some individuals may exhibit gastric intolerance to even therapeutic amounts. Allergic reactions associated with acute overdosage should be handled in the usual manner—that is, by the administration of adrenalin, corticosteroids, and antihistamines as indicated and the prompt elimination of unabsorbed drug, in addition to all needed supportive measures.

How supplied: 250 mg—in bottles of 100 and in unit-dose packages of 100 enteric-coated tablets. Caution: Federal law prohibits dispensing without prescription.

For additional product information, consult the package insert or see your Upjohn Representative.

emonstrated bioequivalence of E-Mycin taken immediately after meals or between meals.



Regimen A (after meals)—One 250 mg E-Mycin® tablet administered q.i.d. immediately after breakfast, lunch, and dinner, and at bedtime with a snack.

Regimen B (between meals)—One 250 mg E-Mycin tablet administered q 6h at least two hours after meals.

E-Mycin Study CS076 on file at The Upjohn Company. The study was performed with twenty-two normal male adult volunteers utilizing a randomized two-way complete crossover design.

statistically significant difference in area under curve was observed from 0-24 hours or 48-72 rs at the 95% confidence level (p>.05).

data clearly demonstrate that E-Mycin, when inistered q.i.d. immediately after meals, proed average serum levels equivalent to those ained when the drug was administered q 6h at t two hours after meals.

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Formulated for quality . . . priced for economy

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MED B-7-S

Opinion & Dialogue

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration

The idea of a so-called patient package insert has been around for a long time. Many physicians alread use written instruction sheets to provide patients with information about the drugs they are taking. An some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit wit glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official packag insert for patients is a good one. Perhaps we should really think of this kind of information simply as a extension of drug labeling.

The benefits of patient involvement

Many physicians may not rea ize how frequently a patient obtai his drug information from Aunt Tillie or the next door neighbor. A this information is almost alway bad or irrelevant to the case at ha Furthermore, the incentive to go along with a prescribed program i slim if the only reading matter the patient receives, along with his pr scription, is a bill.

As an educator I am impress by the principle that the best way get someone to do something is t involve him in the process. So the

Dr. James H. Sammons
Executive Vice President
of the American
Medical Association

I think there are advantages well as some real disadvantages i a patient package insert. When y begin to use semi-medical or me cal terms to describe complicati or possible sequelae of disease o treatment, you may frighten the tient—particularly since the mor highly sophisticated patient is n the one who is going to read the i sert. The patient who will read it the one most susceptible to frigh and confusion by the language.

On the positive side, a pack insert will probably give the pati better insight into why he is bei treated the way he is, and it may give the physician a little bit mo time. But it does not remove fro the physician the need or obliga to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should warned of the possibility of seri side reactions—to know what th real dangers are. But it doesn't bit of good to indicate that a pa on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. think the real danger is that fri engendered by the insert may p sibly outweigh the potential go nain purpose of drug information or the patient is to get his cooperaion in following a drug regimen.

reparation and distribution of atient drug information

We would hope to amass infornation from physicians, medical ocieties, the pharmaceutical indusry and centers of medical learning. he ultimate responsibility for uniorm labeling must, however, rest vith the Food and Drug Administraon. There is nothing wrong with nis agency saying, "this informaon is generally agreed upon and nerefore it should be used," as long s our process for getting the infornation is sound.

Distribution of the information a problem. In great measure it ould depend on the medication in uestion. For example, in the case an injectable long-acting progesrone, we would think it mandatory issue two separate leaflets—a hort one for the patient to read bere getting the first shot and a long ne to take home in order to make a ecision about continuing therapy. this case, the information might put directly on the package and t removable at all. But for a meditlon like an antihistamine this formation might be issued sepately, thus giving the physician the tion of distribution. This could eserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socio-economic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

---

ly the doctor can remove that fear 20 or 30 minutes of conversation.

I'm not suggesting that we hhold any information from the tient because, first of all, it would totally dishonest and secondly, it uld defeat the very purpose of the ert. I do think that a patient on the th control pill should know about incidence of phlebothrombosis.

If you're going to tell a patient incidence of serious adverse reions, then you have to tell him t a concerned medical decision s made to use a particular mediion in his situation after careful nsideration of the incidence of nplications or side effects.

otionally unstable patients pose ecial problem

There are patients who, bese of severe emotional problems, ld not handle the information tained in a patient package in. Yet if we are going to have a kage insert at all, we just can't e two inserts. I think we might ply have to tell the families of se patients to remove the insert n the package.

al implications of the patient kage insert

Just what effect would a patient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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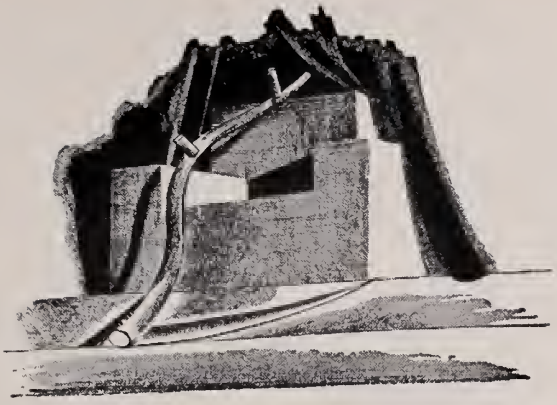

In Memoriam

PATRICK G. H. J. BOSLEY, M.D.

Dr. Patrick Bosley, 47, former Lyon County Health Officer and outspoken foe of agricultural pollution, died July 15.

He was born in Somerset, England, and attended Oxford University. He came from medical-school teaching in the West Indies in 1966 to Balaton, a small community in Lyon County in southwestern Minnesota. After leaving Balaton in 1973, he was an assistant professor in the School of Medicine at the University of Iowa at Iowa City, and was on the staff of a hospital in Muscatine, Iowa.

Since August, 1974, Dr. Bosley had been on the staff of the Sister Kenny Institute in Minneapolis, of which he had been a director for several years.

His wife, Jean, and six children, survive him.

JEROME TEXTOR, M.D.

Dr. Jerome D. Textor, 64, Champlin internist, died May 22. He was a former Chief of Medical Services, Anoka State Hospital, active at Glen Lake State Sanitarium until his retirement three years ago, member of the American Medical Association and East Central Minnesota Medical Society and an Associate Member of the Minnesota State Medical Association. His medical education had been obtained at Stritch Medical School.

Dr. Textor is survived by his son, Dr. Stephen Textor of Boston, and daughter, Susan.

RICHARD I. DORGE, M.D.

Dr. Richard I. Dorge, 88, Minneapolis otolaryngologist, died February 8. He was a graduate in medicine from the University of Minnesota Medical School in 1913.

Dr. Dorge was an active member of the Hennepin County Medical Society, a member of the American Medical Association and a 50 Club and Life Member of the Minnesota State Medical Association.

WILLIAM F. BRAASCH, M.D.

Dr. William F. Braasch, 96, the 12th physician to join the Mayo Clinic, died May 1. He was the last surviving physician who had started his career with the late Drs. Will and Charlie Mayo, founders of the clinic.

An urologist, he was the founder of the Olmsted Community Hospital. He developed some of the urologic instruments used today and served as president of scores of national and international urologic associations. In addition, he helped establish the American Board of Urology. Born in Lyons, Iowa, he received his medical education at the University of Minnesota. He was a former president of the Minnesota State Medical Association, a member of the American Medical Association's House of Delegates for 12 years, and a member of the Zumbro Valley Medical Society. Dr. Braasch was also a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by a son, Dr. John Braasch of Boston, and two daughters, Marian and Elizabeth.

MARY C. GHOSTLEY, M.D.

Dr. Mary Ghostley, 93, pioneer physician in the International Falls Area, died April 9. She taught school to earn money to go to Hamline University where she graduated in 1909 as a Doctor of Medicine. She went to International Falls in 1910 and remained in the area until 1929. She then moved to the Bemidji area where she became the superintendent and medical director of Lake Julia Sanatorium, a center for tuberculosis cases, where she stayed until it closed in 1953. At that time she was appointed Medical Director for the First District, Minnesota Health Department, where she remained until 1961.

Dr. Ghostley was a member of the American Medical Association and the Upper Mississippi Medical Society, and a Life and 50 Club Member of the Minnesota State Medical Association.

She is survived by a son, Dr. James Ghostley of Bemidji, and a daughter, Mary Catherine.

PAUL W. BRANSFORD, M.D.

Dr. Paul Bransford, 58, Minneapolis psychiatrist, died June 30. He was a Clinical Associate Professor of the Department of Psychiatry, University of Minnesota Medical School. Born in Dayton, Ohio, he attended Harvard Medical School.

Dr. Bransford was a member of the Hennepin County Medical Society, the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, Ann, and four children.

IN MEMORIAM

RICHARD BERG, M.D.

Dr. Richard Berg, 58, Hutchinson psychiatrist, died March 9. He was born in Waterville, Washington, and was a member of the McLeod County Medical Society, the American Medical Association and the Minnesota State Medical Association.

Dr. Berg is survived by his wife, Millicent.

GEORGE LOEB, M.D.

Dr. George Loeb, 62, St. Cloud radiologist, died May 29. He was born in Goettingen, Germany, and obtained his medical education at the Medical Faculties of Universities located at Freiburg and Goettingen, Germany. His post-graduate work was completed at the University of Minnesota Medical School.

He was a member of the Stearns-Benton County Medical Society, the American Medical Association, and the Minnesota State Medical Association.

Dr. Loeb is survived by his wife, Hannah, and five children.

JAMES A. BLAKE, M.D.

Dr. James A. Blake, physician, died August 27. He was 66 years of age. In 1954 he was given the highest annual honor bestowed by the American Academy of General Practice, Minnesota Chapter.

He was a former president of the Minnesota Academy of General Practice, past chief of staff of Eitel Hospital, former president of the Hennepin County Medical Society. Since 1960 he has been chairman of the Physician's Assistance Committee of the Minnesota State Medical Association. He was also First Vice President of the Minnesota State Medical Association Foundation in 1973. In addition he was a member of the American Medical Association.

Dr. Blake is survived by his wife, Ruth.

LEON H. FLANCHER, M.D.

Dr. Leon H. Flancher, Crookston Tuberculosis Specialist, died August 4. A 1910 graduate of Marquette University School of Medicine, Dr. Flancher was in private practice for many years before becoming affiliated with the Milwaukee County T.B. Sanitarium. He was superintendent and medical director for the Sand Beach Sanitorium at Lake Park from 1925-41, and from 1951-59 he was superintendent and medical director of the Sunnyrest Sanitarium in Crookston. He also served as epidemiologist in charge of tuberculosis for a time for the Minnesota Department of Health.

He was a member of the American Medical Association and the Red River Valley Medical Society and a Life and 50 Club Member of the Minnesota State Medical Association.

Dr. Flancher is survived by his wife, Anna, a son, Leon, and a daughter, Mary Ellen.

CARLETON WALTER LEVERENZ, M.D.

Dr. Carleton Walter Leverenz, 71, St. Paul physician died July 21. His medical education was obtained at the University of Illinois College of Medicine and his specialty was neuropsychiatry.

He was a member of the American Medical Association Ramsey County Medical Society and the Minnesota State Medical Association.

Dr. Leverenz is survived by his wife, Carolyn, and son, Craig.

EINER WESLEY JOHNSON, M.D.

Dr. Einer W. Johnson, 93, Bemidji community leader, physician and resident for the past 63 years, died June 26.

Born in Greenlead, Minnesota, he attended Hamline Medical School and later fulfilled post-graduate work at the University of Edinburgh, Scotland. Here he was awarded the title of Licentiate of The Royal College of Surgeons, Edinburgh.

He was a member and former president of the Upper Mississippi Medical Society, a 50 Club and Life Member of the Minnesota State Medical Association, and a member of the American Medical Association. A member of all Masonic bodies, he served as the Right Eminent Grand Commander for Minnesota in 1962, one of the highest honors attainable in that organization.

His daughter, Martha, and a son, Dr. E. W. Johnson, Jr. of the Mayo Clinic survive him.

BENJAMIN BOFENKAMP, M.D.

Dr. Benjamin Bofenkamp, 57, Minneapolis otolaryngologist, died July 29. He was a graduate of the University of Minnesota Medical School.

Dr. Bofenkamp was a member of the Minnesota State Medical Association, American Medical Association and the Hennepin County Medical Society.

He is survived by his daughter, Nan Jean, and sons, James and Joseph.

LOUIS A. BUIE, M.D.

Dr. Louis A. Buie, founder of Mayo Clinic's Section of Proctology, died July 2. He had been a member of the Clinic staff for 36 years until his retirement in 1955.

Dr. Buie was born in Kingstree, S.C. and earned his doctor degree from the University of Maryland in 1915. He came to Rochester in 1917 as a resident in surgery.

He was the founder of the American Board of Proctology, later serving as secretary and president. In addition he was president of the American Proctologic Society, the Minnesota State Medical Association, the Zumbro Valley Medical Society and was chairman of the section of gastroenterology and proctology of the American Medical Association. He helped design instruments to help improve treatment and examinations, including a sigmoidoscope for examining the colon and a proctoscopic table. He also designed forceps for taking specimens of tissue for biopsy. Dr. Buie was a former delegate to the American Medical Association.

He is survived by his wife, Zelma, daughter, Nancy, and son, Dr. Louis Buie, Jr. of Minneapolis.

ROBERT E. FRICKE, M.D.

Dr. Robert E. Fricke, 83, Rochester radiologist, died August 4. He had been a consultant, Section on Therapeutic Radiology, the Mayo Clinic.

A Johns Hopkins Medical School graduate, Dr. Fricke interned at Howard A. Kelly Hospital in Baltimore, Maryland.

He was a member of the American Medical Association and the Zumbro Valley Medical Society and a Life and 50 Club Member of the Minnesota State Medical Association.

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The physician should be alert to the earliest anifestations of thrombotic disorders (throm phlebitis, retinal thrombosis, cerebral embolism and pulmonary embolism). If these occur or are suspected, estrogen therapy should be discontinued immediately.

Estrogens may be excreted in the mother's milk and an estrogenic effect upon the infant has been described. The long range effect on the nursing infant cannot be determined at this time.

Hypercalcemia may occur in as many as 15 percent of breast cancer patients with metastases, and this usually indicates progression of bone metastases. This occurrence depends neither on dose nor on immobilization. In the presence of progression of the cancer or hypercalcemia, estrogen administration should be stopped.

A statistically significant association has been reported between maternal ingestion of diethylstilbestrol during pregnancy and the occurrence of vaginal carcinoma in the offspring. This occurred with the use of diethylstilbestrol for the treatment of threatened abortion or high risk pregnancies. Whether or not such an association is applicable to all estrogens is not known at this time. In view of this finding, however, the use of any estrogen in pregnancy is not recommended.

Failure to control abnormal uterine bleeding or unexpected recurrence is an indication for curettage.
Precautions: As with all short acting estrogens, the following precautions should be observed:

A complete pretreatment physical examination should be performed with special reference to pelvic and breast examinations.

To avoid prolonged stimulation of the endometrium and breasts in climacteric or hypogonadal women, estrogens should be administered cyclically (3 week regimen with 1 week rest period—withdrawal bleeding may occur during rest period).

Because of individual variation in endogenous estrogen production, relative overdosage may occur which could cause undesirable effects such as abnormal or excessive uterine bleeding, mastodynia and edema.

Because of salt and water retention associated with estrogenic anabolic activity, estrogens should be used with caution in patients with epilepsy, migraine, asthma, cardiac, or renal disease.

If unexplained or excessive vaginal bleeding should occur, reexamination should be made for organic pathology.

Pre-existing uterine fibromyomata may increase in size while using estrogens; therefore, patients should be examined at regular intervals while receiving estrogenic therapy.

The pathologist should be advised of estrogen therapy when relevant specimens are submitted.

Because of their effects on epiphyseal closure, estrogens should be used judiciously in young patients in whom bone growth is incomplete.

Prolonged high dosages of estrogens will inhibit anterior pituitary functions. This should be borne in mind when treating patients in whom fertility is desired.

The age of the patient constitutes no absolute limiting factor, although treatment with estrogens may mask the onset of the climacteric.

Certain liver and endocrine function tests may be affected by exogenous estrogen administration. If test results are abnormal in a patient taking estrogen, they should be repeated after estrogen has been withdrawn for one cycle.
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(Continued on page 65

School Screening for the Early Detection of Spine Deformities

Progress and Pitfalls

JOHN E. LONSTEIN, M.D.,* ROBERT B. WINTER, M.D.,* JOHN H. MOE, M.D.,†
ANTHONY J. BIANCO, M.D.,‡ RONALD G. CAMPBELL, M.D.#
and MILDRED A. NORVAL, M.D.δ

A year ago a program was outlined in the state of Minnesota for the routine school examination of children for the early detection of spine deformities. This routine examination has been established and in the 1973-1974 school year 80,144 children were screened (approximately 25% of the sixth, seventh, and eighth grade children). 9.1% of girls and 6.5% of boys were found to have rib humps on the forward bending test. Half of these were referred to a physician for a standing Xray and more detailed evaluation. Significant and progressive curves were referred onward for orthopaedic treatment. With this program of early detection, major, expensive, and sometimes hazardous surgery can usually be prevented by early bracing.

A YEAR AGO "A Plea for the Routine School Examination of Children for Spine Deformities" was made by the senior authors in this Journal.[12] This report confirms the need for such a program, outlines the progress of this program, gives some of the information obtained, and highlights some of the pitfalls and problems of such a program.

Need for Early Detection

Why do spine deformities need to be detected early? Spine deformities are still allowed to progress and present late for treatment. When progression of a deformity occurs, it continues hroughout the adolescent growth spurt and may esult in a severe deformity. In the thoracic area he chest cage is deformed with reduced pulmoary function and later cor pulmonale and early eath.[8,9] In the lumbar area the altered biomehanics result in degenerative arthrosis of the acet joints with back pain which can be incapactating. These problems do not occur with every ase of scoliosis, but only in the untreated pro-

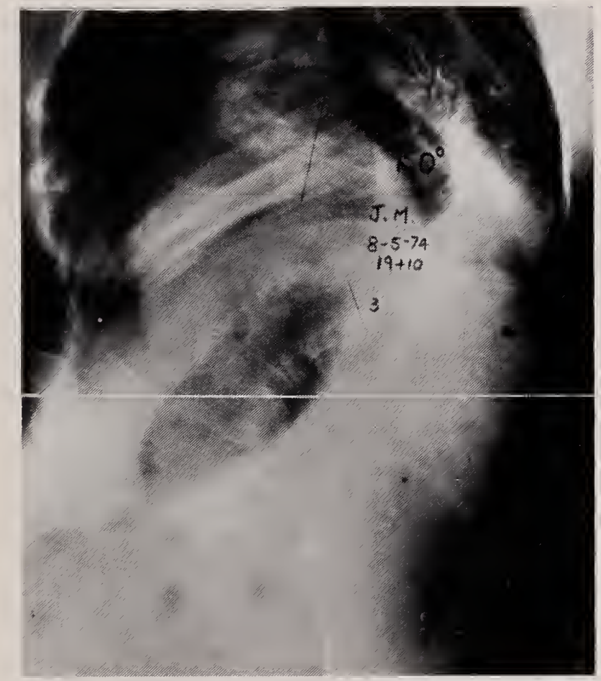

Fig 1—19+10-year-old female who had scoliosis noted at age 14. This was inadequately treated and allowed to progress to a 150 degree right thoracic curve on presentation. Pulmonary functions were reduced to 33% of normal. A multiple stage corrective procedure was undertaken but she died suddenly of massive pulmonary emboli on the morning of one of the surgical procedures. This could have been prevented by adequate early care.

---

*The Scoliosis Service of Gillette Children's Hospital.
†Director of the Twin Cities Scoliosis Center, Minneapolis.
‡Department of Orthopedic Surgery, Mayo Clinic.
#Director of Maternal and Child Health, Minnesota Department of Health.
δDirector Crippled Children's Services Minnesota Department Health.

gressive curves which are severe at the end of growth.

There is a need for early detection of spine deformities. Cases are still seen for the first time at the Twin Cities Scoliosis Center too late for treatment or where treatment is difficult and frought with hazards. In 1974, eight of these patients died. Of these eight, six had documented progression and six died of pulmonary complications. One of these is a female who presented at the age of nineteen with a 150° idiopathic scoliosis (Figure 1). This was first noted at the age of fourteen but allowed to progress. A multiple stage correction was undertaken, but she died of pulmonary emboli during the treatment. If these curves had been detected early, not allowed to progress, and treated early, multiple surgical procedures and their hazards would not have been necessary.

History

How can these spinal curvatures be detected early? As they occur commonly in adolescents, examination yearly during these years would detect the deformities early when the curves are small and amenable to non-operative brace treatment. The easiest way to achieve this is with yearly school screening during the years at risk (grades five through eight or ages 10-13).

Orthopedic screening of school children was introduced in Delaware in 1962.[4] Children were screened for all orthopedic problems including scoliosis. The screening for scoliosis spread to other states over the next fourteen years. These and other studies have shown a prevalence rate of .18% to 3.7%.[3,5,6,10,11,13]

A recent report by Brooks on an examination of 841 school children showed an incidence of scoliosis of 11%, with the average size of the curve being 13°.[1] An extension of this study with 2,500 children showed the incidence to remain 11% and a female to male ratio of 3 to 2.[2] This nearly equal sex incidence is different from the five to one ratio found in the literature.

Several years ago in Minnesota, school screening for spine deformities was started on a small scale in a few school districts. The program gradually spread and is now on a state wide basis. This routine examination of school children for spinal curvatures has been given the approval of the Minnesota State Medical Association. It differs little from the school screening performed for eye and ear problems.

The importance of the screening program is shown in this recent statement of the American Academy of Orthopaedic Surgeons (July, 1974).

"The American Academy of Orthopaedic Surgeons hereby gives its official recommendation to any program of routine examination of school children for the detection of scoliosis and other crippling spine deformities. The Academy recognizes that by early detection more appropriate treatment can be given and a better total treatment of this disabling health problem can be carried out."

Screening Program Technique

The goal of the program is the early detection of spinal curvatures while the curves are small and amendable to treatment with a brace. Children in the years at risk (grades five through eight, ages 10-13) are examined yearly at school by the school nurse or school physical education teachers.

The screening staff is instructed in the basics of spine deformities and the method of screening by the use of regional workshops. These regional workshops are held statewide under the auspices of the Minnesota Department of Health and the Minnesota Department of Education. The physicians of the Spine Service of Gillette Children's Hospital and the Mayo Clinic instruct the staff in proper examining technique, including the forward bending test (Figures 2A, B, C and D). This test can detect small curves virtually impossible to see on a routine visualization of the back in the standing position.

The child is examined bare backed or is clothed

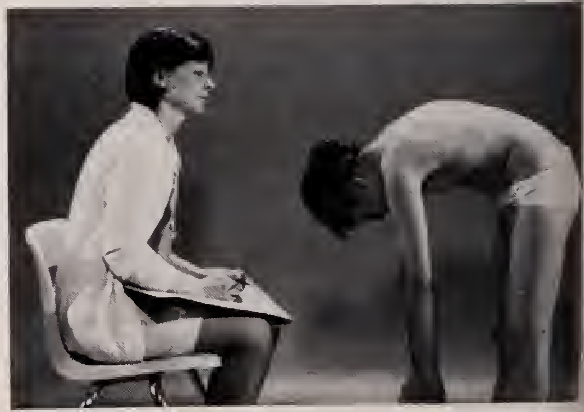

Fig. 2A—A female, age 12 years + four months. Back view showed no obvious deformity. This illustration shows the forward bending test, sideview. Child bend forward at the waist and stands with knees straight, arm hanging, and palms and fingers together. The examine looks down the child's back, from the head end.

in a plain colored tight fitting top. The child bends towards the examiner and stands with the knees straight, arms hanging and palms and fingers together. The two sides of the chest and lumbar area should be absolutely symmetrical and level. The two sides are compared and any difference is abnormal and may be an indication of a scoliotic curve with a rotational prominence. It is important that the knees are straight and arms dependent, not resting on the legs, and hands must be together—any variation in the position in forward bending may cause the back to be twisted and give a false impression of a curvature.

The screening is usually performed in a physical education class by the school nurse and physical education teacher. In this way, a large number of children can be screened in a short time—in fact, only thirty seconds are needed to screen each child. If a possible curvature is detected the child is given a slip of paper to be taken home and given to the parents or guardian. This paper

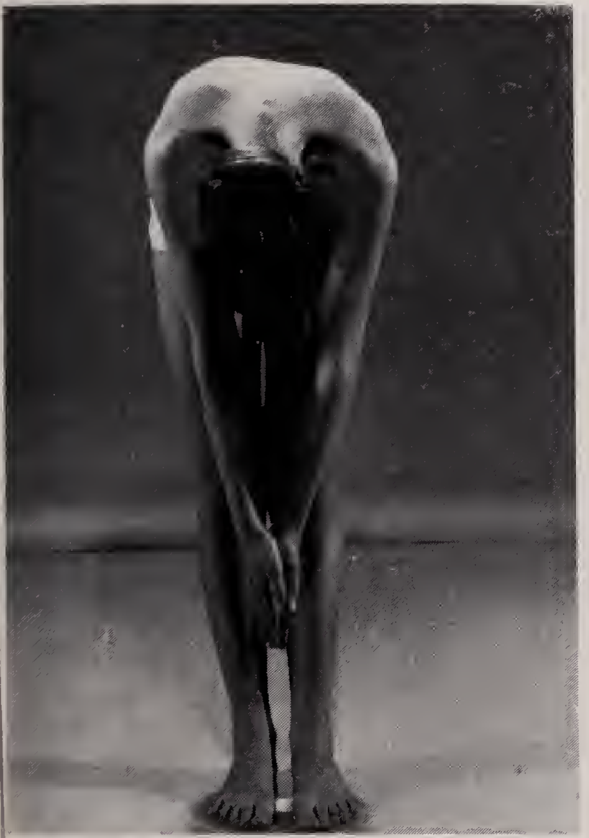

Fig. 2B—Examiners view of child on forward bending test. Note that the knees are straight, arms dependent and hands held with palms and fingers together. The two sides of the thoracic area should be level and symmetrical—note the rotational rib prominence ("hump") on he child's right.

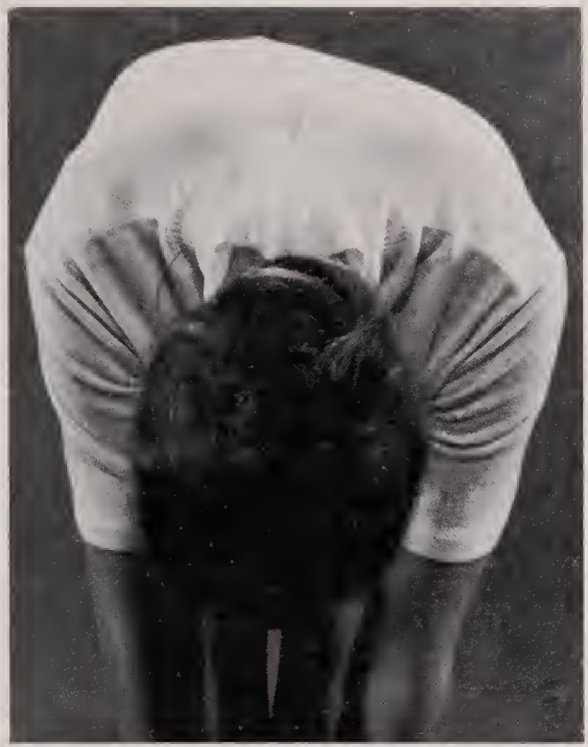

Fig. 2C—Forward bending test with the child clothed in a plain colored T-shirt (no stripes, checks, or patterns). The prominence on the right is still easily detectable.

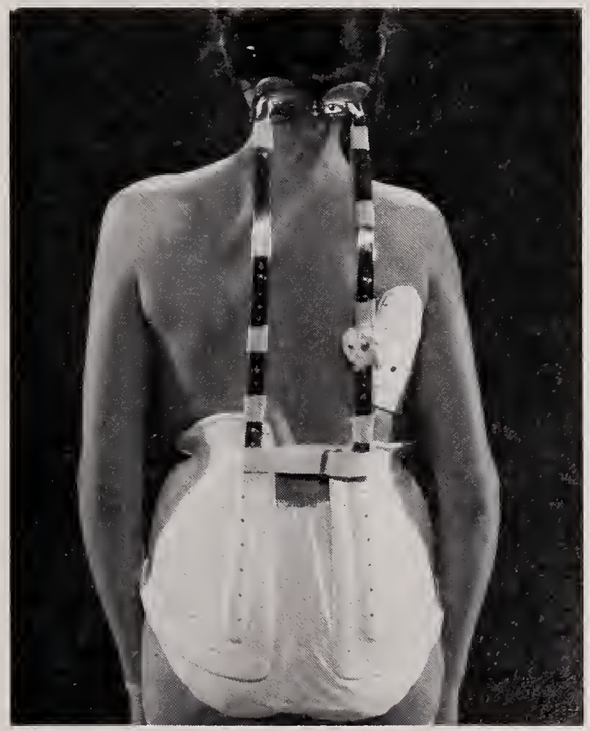

Fig. 2D—Xray showed a 21° right thoracic curve. A Milwaukee brace was fitted. This back view shows the snuggly fitting pelvic girdle with uprights and the right thoracic pad to correct the curve. After five months the brace corrected the curve to 11°.

recommends that the child be seen by the family physician or pediatrician to evaluate the possible curvature by further physical examination as well as a *standing* antero-posterior Xray of the spine. If a curvature is confirmed, the physician usually refers the child to an orthopedic surgeon, the Crippled Children Field Clinic, Gillette Children's Hospital, the University of Minnesota, or the Mayo Clinic.

Results of Screening

In Minnesota in the 1973-1974 school year, the routine school screening for spine deformities was established on a state wide basis. As this was the first year of the state wide program, only ± 25% of the school children (in grades 5-8), or 80,144 were screened (Table 1). Rotational rib prominences or positive forward bending tests were found in 6,251 children with an incidence of 6.5% in boys and 9.1% in girls. Of these 2,742 were referred for further examination including a standing Xray giving 2.5% of boys and 4.3% of girls referred to physicians. Note that the number referred is less than the number who have possible rotation on the screening test. This is because some of the positive tests showed a very small difference. This small rib hump could either not be confirmed on the repeat test, or the difference was questionable and referral postponed until rescreening by the school nurse in four to six months. This nearly equal sex incidence is interesting to note and is a new finding found as a result of the school screening program. This contrasts with the known greater incidence of curves in girls. This indicates an equal sex prevalence of scoliosis, with progresion predominant in females giving a larger proportion of girls requiring treatment.

TABLE 1

Minnesota Screening 1974
Grades 5-10

	Total	Male	Female
Screened	80,144	39,968	40,176
Number rib humps		2,579	3,672
		6.5%	9.1%
Number referred		1,008	1,734
		2.5%	4.3%

In the 1974-1975 school year, the program was expanded and half of the 5th and 6th grades and all of the 7th and 8th grades were examined. Thus, 237,000 or 75% of the children in these grades were examined for the early detection of spine deformities. Additional information regarding the physician's diagnosis and the treatment program—obsevation, bracing, or surgery—that is recommended and followed is also being collected. In this way, the prevalence of scoliosis in the state of Minnesota will be obtained as well as the percentage that require bracing or surgery.

The large prevalence of scoliosis and the increased referral from the screening program is seen in the number of new patients presenting for evaluation to the Spine Service of Gillette Children's Hospital (Table 2). In 1970, there were seventy-seven new patients. Shortly after this, school screening for spine deformities was introduced in some Minnesota schools and the program gradually increased and in 1974—the first year of state-wide school screening—reached 257. The children presenting have either a curve large enough to require active treatment—bracing or surgery—or they are observed. Periodic evaluation including a standing Xray is repeated every four to six months to see if the curvature is progressive, these progressive curves requiring bracing.

TABLE 2
New Scoliosis Patients
Gillette Children's Hospital

1970	77
1971	114
1972	128
1973	207
1974	257

The brace usually used for these curvatures is a Milwaukee brace which has been shown by Moe and Kettleson to be effective in partially correcting the curvatures and preventing the curvature from progressing further.[7] Occasionally after partial correction, the curve progresses in spite of the brace, and surgical correction and fusion is necessary. The brace is worn full time until completion of growth, and then gradually removed. In the cases detected by the school screening program, a large number of flexible lumbar and thoraco-lumbar curves have been found, in contrast to the higher incidence of thoracic curves reported previously. Hall from Boston Children's Hospital has introduced a brace without a neck-ring or uprights for this specific group of flexible, low curves. This thoraco-lumbar-sacral-orthosis (TLSO) works like the Milwaukee brace, on the three point fixation principle having a "built-in" pad for the apex of the lumbar curvature (Figures 3A, B, C). The TLSO has been well received by patients and early results are promising in terms of excellent correction of the curves in the brace.

An interesting case detected by the screening program is C. R. (Figure 4). He is a thirteen and a half year old boy found to have a left lumbar prominence. Initial evaluation by his local physician including a standing Xray showed a congenital scoliosis. He was referred to Gillette Children's Hospital for treatment. As with all congenital spine deformities, an intravenous pyelogram was performed as 14-20% of congenital scoliosis patients have renal tract abnormalities. The IVP showed hydronephrosis on the right due to uretero-vesical obstruction. There was reduced renal parenchyma on the right and normal renal function. A ureteral reimplantation was performed before the scoliosis treatment was started. There is no doubt that the detection of this case of scoliosis resulted in detection of the renal abnormality that with time would have been life threatening if untreated.

Education

The aim of the school screening program for

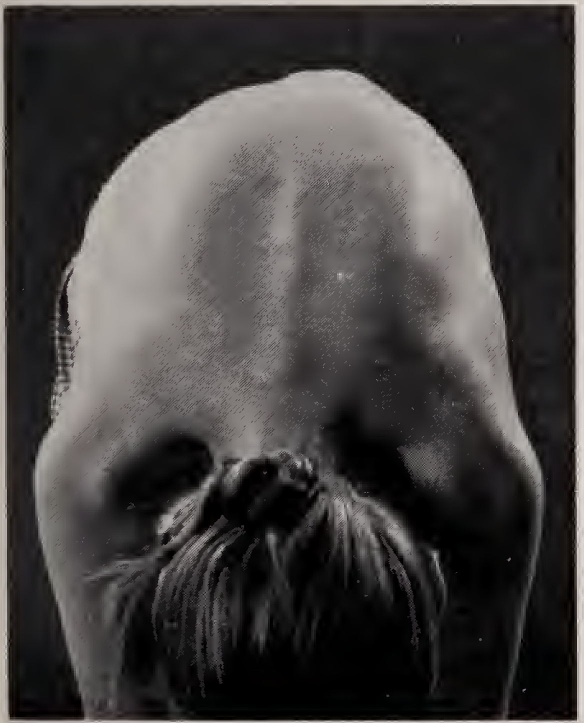

Fig. 3A. This 11+10 year old girl shows on the forward bending test an abnormal lumbar area. Note the left side is higher than the right due to a lumbar rotational prominence. The rotated vertebrae causes the paravertebral muscles to be prominent on one side.

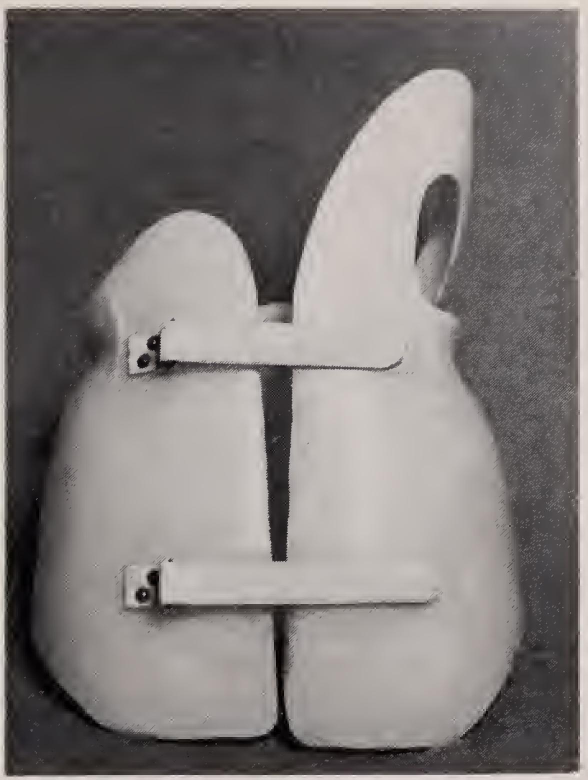

Fig. 3B—The thoraco-lumbo-sacral-orthosis—TLSO. This is fabricated from polypropylene with a built in pad posteriorly on the left to press on the convexity of the curvature. There is an extension in the right axilla for counterpressure.

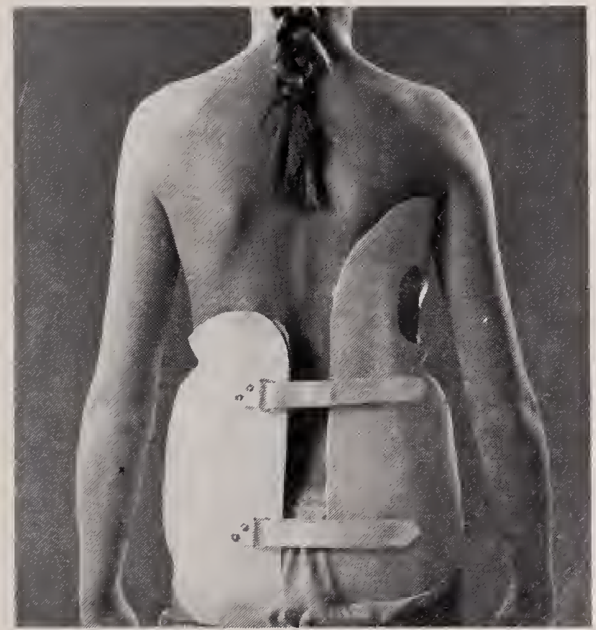

Fig. 3C—Female in the TLSO (back view). Standing Xray initially showed a 17° left lumbar curve which progressed to 22°. After TLSO was fitted patient was placed in the brace and after two hours the curve corrected to 12°. Note the snug fit of the brace, absence of the uprights, and excellent cosmetic appearance.

spine deformities is the early detection of these curvatures with treatment by bracing, thus, preventing progression of these curvatures and avoiding the dangers and expense of surgery. To help educate the screening staff at the regional workshops a booklet has been prepared, and is issued to all in attendance. In addition, a fifteen minute movie has been completed which can be shown to school staff, parents, PTA's, and the general population, increasing their awareness of scoliosis and pointing out the dangers of untreated progressive curvatures. A scientific display was presented at the 1974 State Medical Association meeting outlining the school screening program. With the use of these educational aids it is hoped to detect all spine deformities early through school screening, and eliminate the need for most surgical intervention in idiopathic scoliosis. The success of such a program has been shown in Delaware during the past ten years, and now there are virtually no children in Delaware that require surgical correction and fusion for idiopathic scoliosis.

Pitfalls and Errors

The experience gained through the state wide screening program in Minnesota has presented many pitfalls and errors.

1. Over Call by School Nurse. The inexperienced school nurse with enthusiasm for the screening program may over diagnose rotational prominences. This may occur if the screening position is not standardized or if the eye is not yet trained to detect the rotational prominences. With experience this "over call" decreases.

2. Under Call by School Nurse. This can also occur with the inexperienced screener. The person screening may, due to lack of knowledge about scoliosis, not wish to have a child placed in a brace. With this doubt in her mind, she may not refer a rotational prominence for evaluation. Education can correct this problem.

3. Failure of Family to Seek Medical Evaluation. The family, on being notified of the possibility of a spine deformity, may fail to seek medical evaluation. This procrastination can allow a deformity to progress and make non operative treatment difficult or impossible. The way to prevent this is to educate the public on spine deformities, emphasizing the possible complications and the need for early care.

4. Poor Counseling by Family Physician. The family physician may make light of the referral, and not examine the child to confirm the rotational prominence. If a prominence is found it may be called a muscle mass or glossed over. The family may be given inaccurate advice about scoliosis and its possible progression.

5. Failure to Obtain Adequate Xrays. The family physician on recognizing a rotational prominence may either fail to take an Xray or may order a supine Xray. The standing Xray is the one necessary to diagnose the deformity and document the amount of the curve.

6. Failure to Recognize Progression. The failure to recognize progression of a scoliotic curve is one of the most common errors in treating scoliosis. Either the Xrays are not accurately measured or the whole series is not reviewed to establish any change that has occurred.

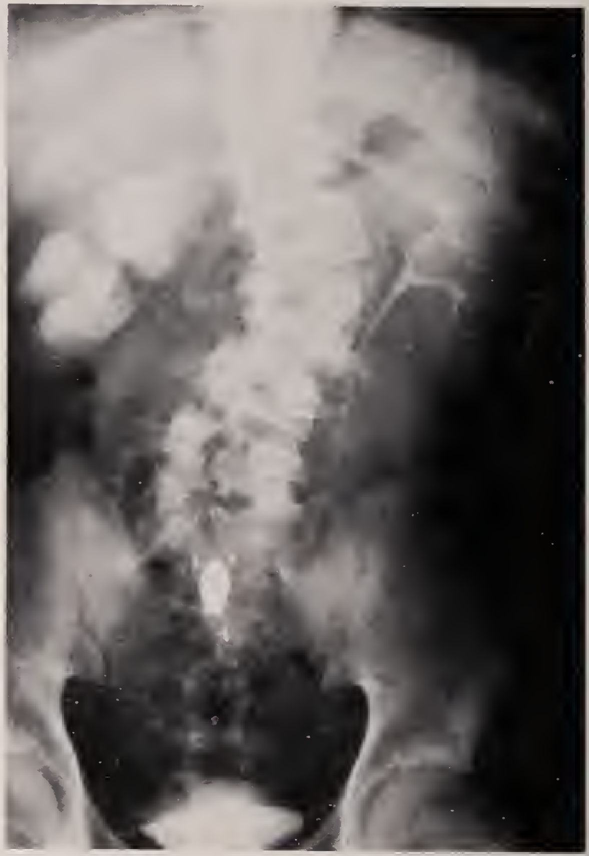

Fig. 4—Thirteen and-a-half-year-old boy diagnosed as having scoliosis on a school screening program. The film showed a congenital scoliosis due to a hemivertebra. The routine intravenous pyelogram showed hydronephrosis on the right due to uretero vesical obstruction. The renal parenchyma is reduced on the right but the renal functions were normal. A re-implantation procedure was successfully performed with reversal of hydronephrosis and future life threatening complication.

Failure to realize that a curve is progressing gives a feeling of security and will prevent referral for definitive care.

7. Failure of Orthopedic Treatment. The last pitfall that can occur is after referral to an orthopaedic surgeon. He may also fail to recognize that the deformity is progressing causing another delay in initiating treatment. With this delay a curve may be observed until it is so advanced as to be impossible to treat in a brace. The brace is effective *only* in mild and flexible curves.

Summary

School screening for the early detection of spine curvatures is now established on a statewide basis in Minnesota in grades five through eight. The incidence of possible curvatures in 80,144 children screened was 2.5% in boys and 4.3% in girls. This nearly equal sex incidence of curvatures is a new finding, as previously scoliosis was thought to predominate in girls. A large number of flexible lumbar and thoraco-lumbar curves have been found and these are responding well to a new brace, the TLSO. The errors and pitfalls that have been found are discussed.

The routine screening of school children is a rapid effective method for early detection of spine deformities. The screening test is simple and takes thirty seconds—"a 30 second investment for a lifetime of dividends."

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Ramsey County Cancer Society Cancer Detection Symposium

Symposium on Cancer Detection is to be held February 19, 1976, at the St. Paul Arts and Sciences Center, 30 East 10th Street, St. Paul, Minnesota.

Malcolm Pike, M.D., Professor of Community Medicine and Pediatrics, University of Southern California, will be the dinner speaker. His topic is that of breast cancer, early detection, and prevention.

This program has been approved for four hours of Continuing Medical Education credits by the Minnesota Academy of Family Physicians. The program will take place in the auditorium in the Arts and Sciences Center on February 19, 1976 with registration beginning at 2 p.m., program to begin at 2:15 p.m., and dinner at 6:00 p.m. The cost of the program is $7.50 per person which includes dinner. The program will conclude at 8:00 p.m. For registration or additional information write or call: Boyd Harris, M.D., Laboratory Dept., St. John's Hospital, 403 Maria Avenue, St. Paul, Minn. 55106.

Mankato Visiting Faculty Seminars

This program is provided through cooperation with the Mayo Clinic. They are held each third Saturday of the month, 9:00-11:00 a.m. in the conference room of St. Josephs Hospital, Mankato. Similar program provided by the University of Minnesota on the second Saturday of the month.

February 21—Dr. D. R. Sanderson "Fiberoptic Bronchoscopy in a Diagnosis of Cancer of the Lung and Foreign Bodies of the Tracheo-Bronchial Tree.

Fracture Conference

Cast Bracing of Femoral Fractures

STEPHEN H. McCOY, M.D.*; EDWARD M. FITZGERALD, M.D.* and
KENNETH A. JOHNSON, M.D.†

Dr. Kenneth A. Johnson:

This conference concerns the treatment of femoral fractures and the principle of immediate weight-bearing as it applies to these fractures. The validity of cast bracing for tibial fractures is unquestioned, but there is doubt about its use for femoral fractures. The traction-spica cast method has been reviewed by Suiter and Bianco[1] in 1971, who stated that skeletal traction through a tibial pin, with balanced support, is the preferred method of closed treatment in adults. They added that, in general, a thigh cannot be immobilized in plaster well enough to prevent displacement unless there is some inherent stability of the fracture, thus implying the necessity of early callus formation. They also mentioned that a problem in the treatment of femoral fractures is determining when it is safe to remove the cast. Although these statements probably were true when they were expressed, I believe that they now are incorrect. Now probably the problem with femoral fractures is not determining when to remove the cast but when to apply the cast.

Case 1

Dr. Stephen H. McCoy:

The first patient is a 13-year-old boy who was hit by a car while riding his bicycle. When seen in the emergency room, he had a fracture (Figure

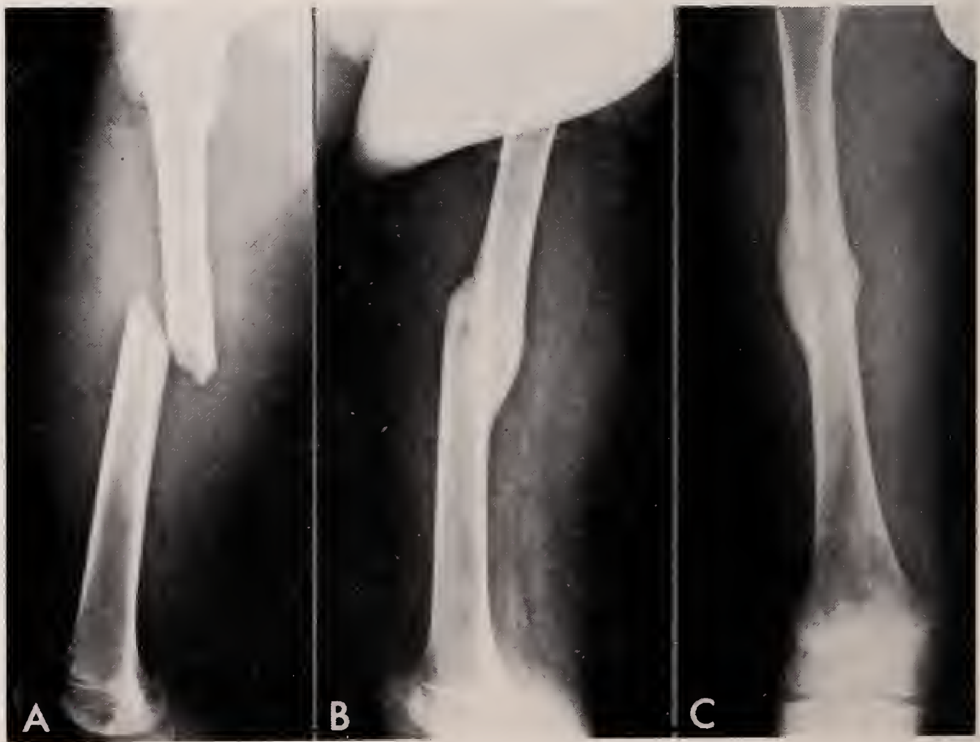

Fig. 1 (case 1)—Midshaft fracture. *(A)* Anteroposterior view in emergency room. Note distal fragment rotation. *(B)* and *(C)*, Result at four months after fracture.

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†Consultant, Department of Orthopedics, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.
Reprint address: Dr. K. A. Johnson, Mayo Clinic, Rochester, MN 55901.
Fracture Conference, Sept. 16, 1974

1 *A*) and no other significant injuries.

Dr. Thomas C. Wilder, Jr.:

The roentgenograms show a short spiral fracture of the midshaft of the proximal femur, with apex angulation medially and bayonet apposition.

Dr. Johnson:

What would you suggest be done in the emergency room to treat this fracture?

Dr. Wilder:

I would put the patient in balanced suspension using a Thomas splint with a Pierson attachment and utilizing a proximal tibial pin for traction.

Dr. McCoy:

A distal femoral Steinmann pin was inserted and the patient was placed in 90/90 traction (the hip was at 90° flexion and the knee at 90° flexion).

Dr. Johnson:

Dr. Klassen, would you comment on the use of a distal femoral pin?

Dr. Rudolph A. Klassen:

I prefer to use a distal femoral pin in fractures of this type because direct traction can be applied to the affected bone without traction stresses crossing the knee joint. If heavy weights are required for a prolonged period with a tibial pin, knee joint stiffness will result. The femoral pin should be inserted about 2 cm proximal to the adductor tubercle, with the knee flexed about 60° to 90°. In this way, the knee joint is not entered and knee stiffness will not be a problem. Previous objections to the use of a femoral pin have been that it causes stiffness and infection of the knee. I believe that, in the studies describing these complications, the pins were placed too far distally and therefore often intra-articularly through the suprapatellar pouch.

Dr. McCoy:

After the patient was in traction for nine days, a long leg cylinder cast was applied, incorporating the femoral pin. The patient began progressive weight-bearing, and he was dismissed from the hospital three days later. The cast was changed at one month following fracture, and a cylinder cast with knee hinges was applied. At two months after fracture, the cast was removed and ambulation with no external support was begun. Dr. Wilder, would you comment on the result?

Dr. Wilder:

I think the result is excellent (Figures 1 *B* and *C*). The alignment and length are satisfactory and, because of the knee motion while in plaster, I would expect knee motion to be full.

Dr. Johnson:

This patient had several factors that were to his advantage in early union of the fracture: he was young; the initial fracture was not greatly displaced, and thus the fracture involved little periosteal stripping or tissue damage; and its position was also reasonably stable. The situation therefore was ideal for fracture healing and I believe that it would have healed by almost any method. With this cast brace method, he was hospitalized for only 14 days; after that, he was totally independent, soon walked without pain, and had an excellent union at two months.

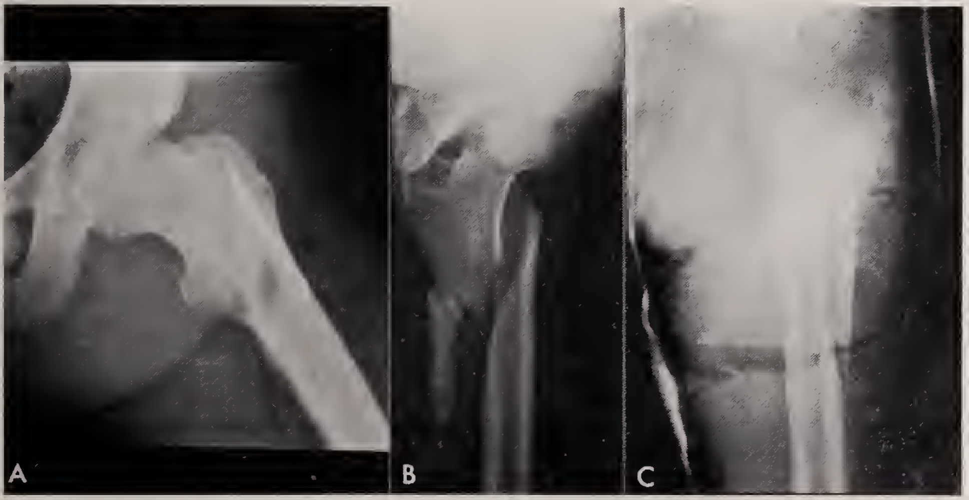

Fig. 2 (case 2)—Subtrochanteric fracture. *(A)* and *(B)* Anteroposterior and lateral views in emergency room. *(C)* Fracture in "mini-spica" at 16 days; cast wedged to correct initial varus deformity.

Case 2

Dr. McCoy:

The second patient is a 19-year-old machinery repairman who was involved in a motorcycle accident. When seen in the emergency room, he had a number of minor injuries and abrasions and a femoral fracture (Figures 2 *A* and *B*). Dr. Lang, how would you classify this fracture?

Dr. Allan G. Lang:

This is a subtrochanteric fracture with comminution. There are three fragments with minimal displacement. I think skeletal traction should be applied with a distal femoral pin.

Dr. Johnson:

The judgment of the admitting surgeon was that operative treatment ultimately would be necessary, so he inserted a proximal tibial pin, thus keeping the traction pin away from the proposed operative region.

Dr. Richard S. Bryan:

I prefer a proximal tibial pin for the treatment of this type of fracture. The problem, just as with a distal femoral pin, is misapplication of the technique. If you insert a tibial pin and burn the bone while you are going through it, then you have tract infection later, with sequestrum formation. And if you apply 35 lb (15.9 kg) through the knee joint, you stretch the ligaments. All treatment methods have their disadvantages, but generally it is the misapplication of the particular method that is the cause of difficulty.

Dr. Johnson:

I agree completely, but I think the belief that a distal femoral pin causes quadriceps contracture problems or stiff and possibly infected knees has been perpetuated unjustifiably. Dr. Klassen has stated, correctly I believe, that the distal femoral pin is not a problem if the pin is inserted more proximal and with the knee flexed. Also, the distal femoral pin serves later as the suspension for casting this fracture, and the knee can be left out of the cast. If you use a proximal tibial pin, then you have to put on knee hinges in order to get the knee moving early.

Dr. McCoy:

Sixteen days after the injury, a "mini-spica" was applied, the proximal tibial pin was removed, and a distal femoral pin was inserted (Figure 2 *C*).

Dr. Johnson:

Note that the fracture initially was in varus, so the cast was wedged. This is a "mini-spica" with a narrow plaster band that goes up around the abdomen. It was put on when the patient was in bed, awake, and with the leg abducted and flexed approximately 30° to 40° in each direction. The cast incorporates the femoral pin but does not extend below the knee; thus, the patient's knee is free to move. After the cast dried, traction was reapplied. The patient was then free to detach his traction by himself, get up and use crutches, put weight on his leg as tolerated, go to the bathroom, and so forth. This was his routine, getting up when necessary but in bed and in traction most of the time.

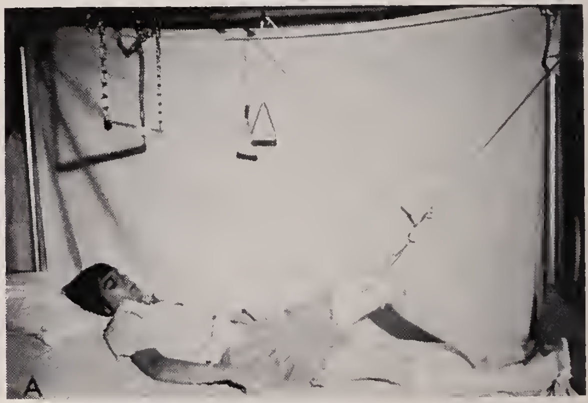

Fig. 3 (case 2)—*(A)* Mini-spica and traction setup for self-disconnection. (By permission of patient.)

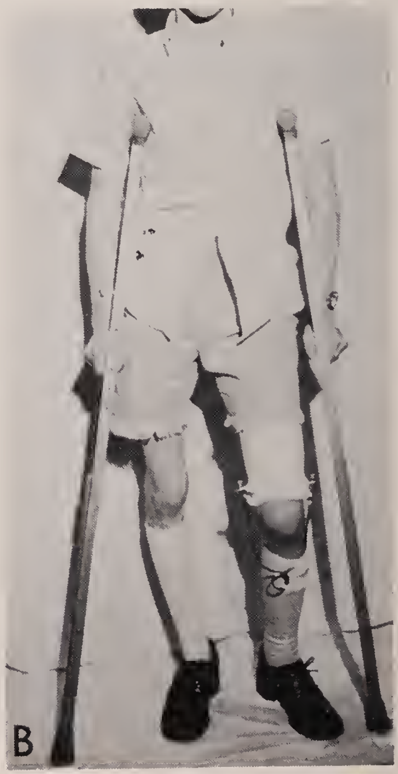

Fig. 3 (case 2)—*(B)* Patient ambulating with traction bow in place.

Dr. McCoy:

The patient was hospitalized in intermittent traction until four weeks following injury (Figures 3 *A* and *B*). Note how he can disconnect the traction by himself.

Dr. Johnson:

Recently, Schweigel and Gropper[2] compared the ambulatory with the nonambulatory treatment of femoral fractures. They found that, in addition to having fewer complications, the early weight-bearing patients were hospitalized an average of 66 days less per patient (saving $4,000 to $5,000 per patient). Total treatment time also averaged seven weeks less for this group.

Dr. McCoy:

Monthly Xrays were taken. The cast was removed 11 weeks after fracture (Figure 4). The reduction was not anatomic but was thought to be satisfactory.

Dr. Patrick J. Kelly:

Dr. Johnson, under what circumstances would you not treat a proximal femoral fracture with a cast brace?

Dr. Johnson:

Many situations are unsuitable for this approach and therefore would need operative treatment or traction and spica cast treatment. A number of studies, mainly concerned with military personnel, have evaluated immediate weight-bearing to all femoral fractures and have found that it could

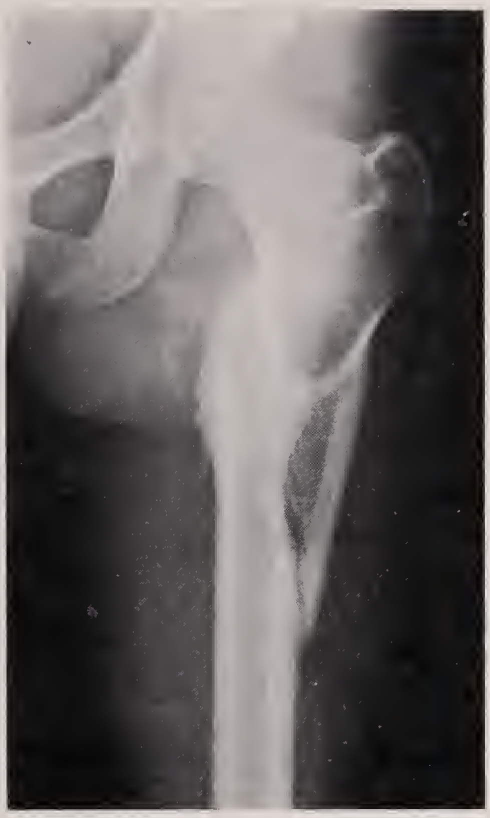

Fig. 4 (case 2)—Healing 11 weeks after fracture.

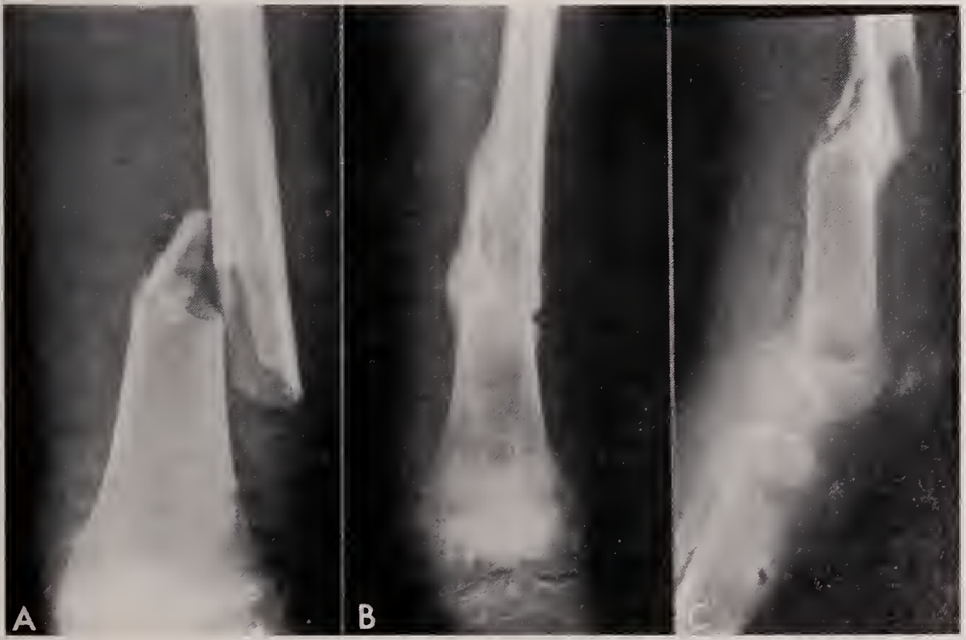

Fig. 5 (case 3)—Supracondylar fracture. *(A)* Anteroposterior view at time of injury. *(B)* and *(C)*. At three months.

not be used in approximately two-thirds of adult femoral shaft fractures. The contraindications included the elderly or infirm, patients who are pregnant or just obese, and those having angina or cardiac failure, hemiplegia, ataxia or parkinsonism, pulmonary insufficiency, major contralateral extremity trauma, major neurologic trauma, severe upper extremity problems, and psychiatric problems.

Dr. Kelly:

How does the cast avoid telescoping of the fracture?

Dr. Johnson:

In the use of the long leg cast brace without the pelvic component, there are two philosophies. The earlier one is that the ischial tuberosity has a major role and that weight is transferred from this tuberosity to the floor.[3] A so-called quadrilateral thigh-bearing (QTB) cast configuration is used to provide this weight transfer. The more recent theory states that the important part is the total contact support of the thigh, with tissue turgor and elasticity supporting the fracture.[4] The later theory does not involve use of a quadrilateral ischial weight-bearing socket and depends solely on a snug, well-molded thigh piece. Pins, when used, act primarily as a suspension for the cast and should be strong.

Case 3

Dr. McCoy:

The third patient is a 16-year-old boy who was injured in a motorcycle accident. His major injury was a fracture of the left femur (Figure 5 *A*).

Dr. Matthew D. Skolnick:

The boy has a comminuted oblique supracondylar fracture of the left femur. I would insert a proximal tibial pin, which would be suitable for a cast brace later.

Dr. Johnson:

Three problems are involved with any femoral fracture when you plan to use a cast brace. In the proximal femur, you tend to get nonunion, although this is rare; in the midfemoral portion, the problem is shortening; and in the distal femur, you get malposition. These three problems should always be considered. Would anyone disagree with the use of a cast brace in this case?

Dr. Bryan:

One could also treat this patient for three weeks in balanced traction suspension and put him in a Delbét-type walking spica cast and have a successful result—that is a single leg spica cast that leaves the ankle free and incorporates the knee joint. Because the patient is 16 years old, I would not expect a stiff knee to develop, so I would not hinge the knee.

Dr. McCoy:

A cylinder cast brace was applied with knee hinges and incorporation of the tibial pin 12 days after injury. The boy was dismissed at one month following injury. The cast was removed at three months after injury (Figures 5 *B* and *C*).

Dr. Johnson:

This type of cast brace has a thigh component, is hinged at the knee, incorporates the tibial pin, and then goes down to above the ankle. The knee, the ankle, and the hip can be moved. I do not think that the knee hinges are the most important parts, but they do make it easier for the patient to move around; and he can sit a bit more comfortably. The essential thing for fracture healing seems to be getting the patient to bear weight on the fracture; whether you use a cylinder with a pin incorporated as in the first case or whether you apply a type like that used in the third case is probably not very important.

Dr. Robert H. Fitzgerald:

Dr. Johnson, I wonder if you have saved the patient much in hospitalization time? Those who use this technique in the so-called standard way apply balanced traction until they see some inherent fracture stability. The patients are in their cast brace by one month, and they are usually out of the hospital a few days later. Two of the three patients discussed in this fracture conference left the hospital at one month. I think if you are going to use the technique early enough to make a difference in time, you are going to have complications such as shortening and displacement.

Dr. Johnson:

We apply the cast after the initial trauma reaction has subsided, which is usually at about two weeks. Then the patient is placed in intermittent traction until he can walk comfortably and after Xrays show no shortening when he is weight-bearing, as opposed to when he is in bed. We try cast wedging to keep angulation to a minimum. The advantage is that the patient can get out of bed much earlier. With this independence, the patient's psychologic outlook is improved. Also, the intermittent fracture loading seems to stimulate fracture healing. Probably, if we had more experience in knowing what to expect and how often to reexamine the patient, and if the patient lived near our institution, we could dismiss him from the hospital shortly after cast application.

Discussion

Dr. Edward M. Fitzgerald:

The forerunner of the cast brace is shown in an illustration from an article by Henry Smith,[5] written in 1855 (Figure 6). This artificial limb, which stimulated the ambulatory treatment of fractures in the western world, utilized the "principle of pressure and motion at the seat of the fracture," thus leading to the stimulation of healing callus.[6]

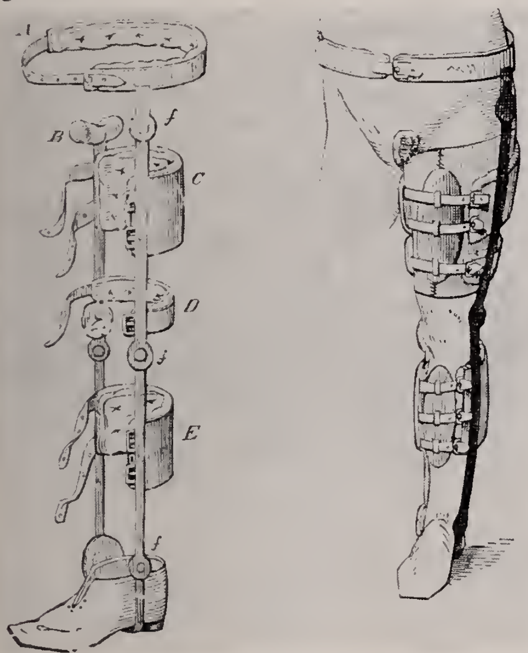

Fig. 6—Artificial limb devised by Henry Smith in 1855. (From Smith HH: On the treatment of ununited fracture by means of artificial limbs, which combine the principle of pressure and motion at the seat of fracture, and lead to the formation of an ensheathing callus: illustrated by the history of four cases of false joint in the femur, eight in the leg, and two in the humerus. Amer J med Sci 29:102-119, 1855 by permission.)

Dr. Steven Smith modified this device and referred to it in his 1887 textbook *Operative Orthopedics*. We now know that cast bracing can work, but is it the motion at the fracture site, the increased blood supply from exercise, or the tourniquet effect of the thigh piece that is most important? This technique, which was born in the 19th century, is stimulating research and affecting patient care in the 20th century.

Dr. McCoy:

Dr. Ernst Dehne began utilizing the weight-bearing principle in 1950, documenting his experience for the first time in 1961 with fractures of the tibia.[6]

The extension of this concept to the femur was a natural process, the validity of which has been amply verified by analysis of results obtained from the walking spica cast, such as those reported by Kaufer[7] in 1972. Hospitalization time in this study averaged 29 days, compared with 58 days in Suiter and Bianco's traction study.[1] Kaufer's complication rate was significant: nonunion in 6.5%, shortening greater than one inch in 5%, pulmonary embolism in 3%, and pressure ulceration in 11%. In addition, Kaufer pointed out that the spica cast: (1) is heavy and clumsy, (2) allows no hip or knee motion, (3) usually does not allow the patient to return to work until after removal, and (4) is applicable to only about one-third of all femoral fractures. Standard nonoperative treatment in isotonic traction is still a safe alternative to internal fixation, though a critical analysis of results reported since 1960 shows significant rates of malunion and nonunion, requiring eventual operative treatment in 11 to 29%, shortening of more than two cm in 14 to 30%, and a refracture incidence of four to 17%.[8]

The ultimate goal of the functional management of femoral fractures is the return of the patient to the best functional state as soon as possible with the lowest morbidity. To accomplish this, we must meet certain anatomic and physiologic prerequisites. Anatomically, a bony union must be achieved without undue shortening or angulation. This is done by traction and cast molding about the thigh to align and gain length, with supplementary traction to maintain leg length. Physiologically, the patient must regain joint motion, muscle strength, endurance, and coordination; these are regained by the active use and assistive knee range of motion, usually via hinging.

In a typical fracture, the cast may be applied anytime from the second day of traction[6] to four or six weeks later, when early fracture stability is noted.[9] Methods of cast brace application have been well described by Mooney[10] and Connolly and King.[8] The use of the QTB socket seems optional, as mentioned by Dr. Johnson. Some surgeons believe that ischial contact must be provided to prevent rotation or trochoidal motion.

Connolly and King demonstrated as much as 43° rotation of the fracture while the patient was in bed traction. This amount of rotation was significantly reduced after cast application.

The approach to the general treatment scheme varies. After initial traction and cast application, the patient is encouraged to walk three to four times each day, after which he goes back into traction. Gravity pulling on the limb via the cast and incorporated pin provides traction when the patient is erect. Connolly and King found that fracture translation associated with traction release is the best indicator of fracture stability. Active patients can learn to disconnect their own traction and rise with little or no assistance. Therefore, the patient participates in a low-risk, fast-recovery program in which he is continually aware of improvement. Bone healing and functional recovery parallel each other throughout. The managing staff must be continually alert for problems, including, at a minimum, weekly Xrays while the patient is hospitalized and monthly Xrays while he is an outpatient.

Multiple studies have shown significantly improved results using cast bracing. Mooney and associates[9] compared two-year post-treatment results in 150 patients who had cast braces with results in 50 controls who had been treated by traction-spica methods. The average healing time for the study group was 14½ weeks, with no nonunions or refractures, whereas that of the control group was 24.7 weeks, with three nonunions and three refractures. Schweigel and Gropper[2] noted similar results in 77 patients. Connolly and King[8] treated 143 fractures in which the healing time was similarly shortened and found a lower complication rate (nonunion or malunion in 0.7%, shortening of more than two cm in 13%, refracture in 2%, and pulmonary embolism in 3%).

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Business Meeting 4:00 P.M.

2nd Annual K. W. Stenstrom Memorial Lecture
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(Continued from page 50)

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Kjell Bergh Borton Volvo, Inc. 6
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Lilly, Eli. & Co. 12
Mallinckrodt Pharmaceuticals 47
Medical Protective Company 6
Pharmaceutical Mfrs. Assn. 42, 43
Roche Laboratories .... Cover 2, 1, 28, 29, 30
Cover 3, Cover 4
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9:45-10:00 a.m.	Welcome Address and Announcements, Dr. Charles Chedister, M.D.
10:00-11:00 a.m.	Pathology of the Pancreas, Roy G. Shorter, M.D.
11:00-11:30 a.m.	Pancreatic Function Testing, Desmond Burke, M.D.
11:30-12:00 a.m.	Diagnosis of Acute Pancreatitis, Eugene P. DiMagno, M.D.
12:00- 1:30 p.m.	Luncheon at Campus Club, Coffman Union
1:30- 2:00 p.m.	Cystic Fibrosis, Warren Warwick, M.D.
2:00- 2:30 p.m.	Functioning Islet Cell Tumors, Laboratory Aspects, Edward Wong, M.D.
2:30- 3:00 p.m.	Sjogren's Syndrome, Laboratory Aspects, Gene G. Hunder, M.D.
3:15- 4:15 p.m.	Tumors of Salivary Glands Benign Tumors, Juan Rosai, M.D. Malignant Tumors, Louis P. Dehner, M.D. Tumor-Like Conditions, Bruce F. Hertel, M.D.

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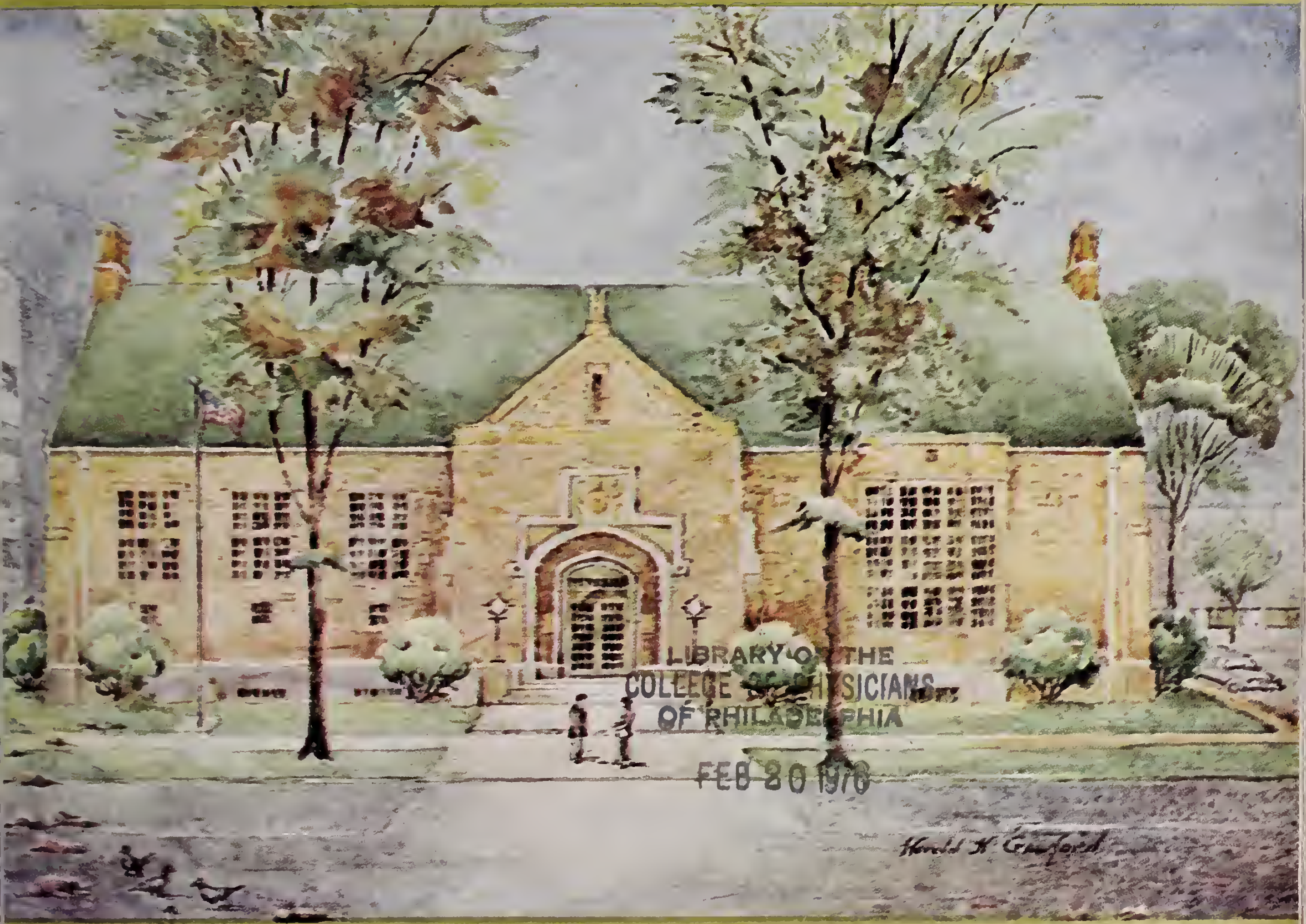

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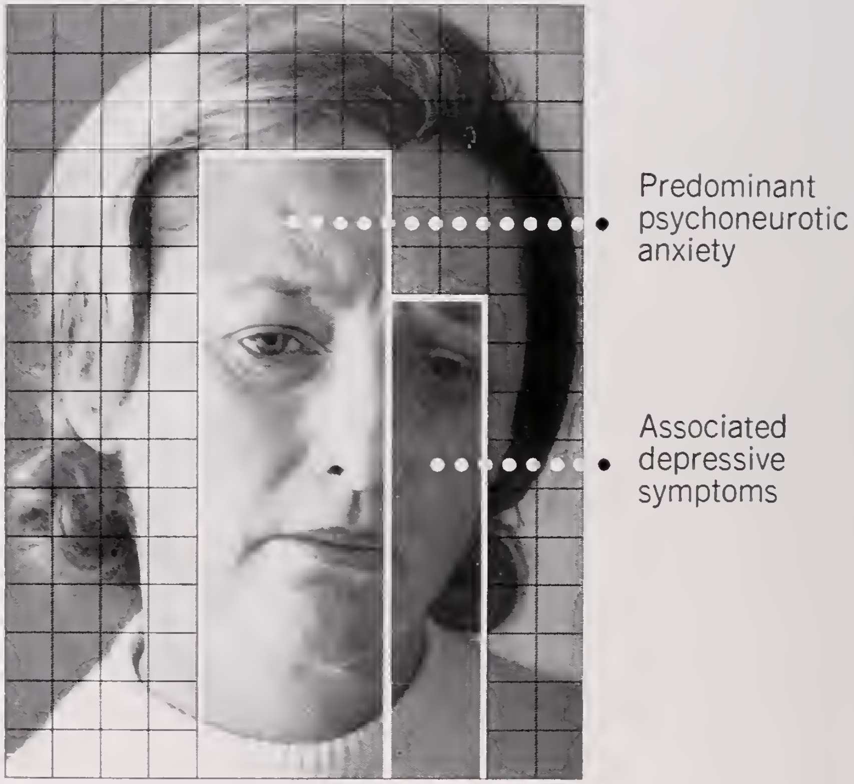
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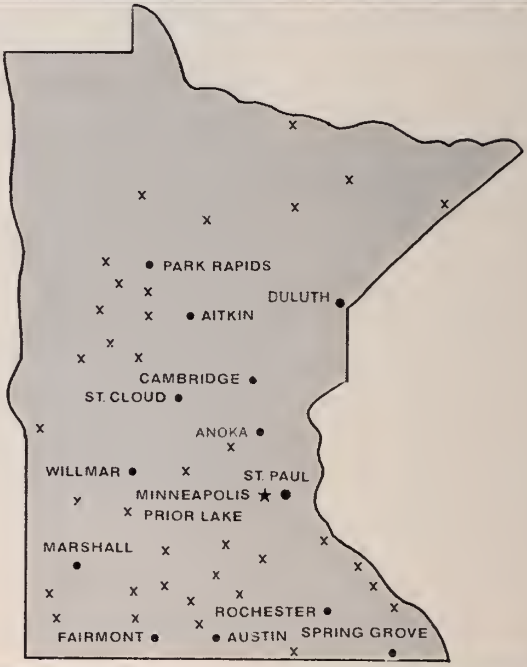

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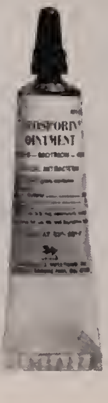

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President's Letter

Participation in Planning

Every member of the Minnesota State Medical Association at this time should be well informed on the implementation of the National Health Planning and Resources Development Act of 1974 (P.L. 93-641). The health service areas designated by the Governor were accepted by HEW in September. Proposed regulations on the designation of Health Systems Agencies (HSA) appeared in the Federal Register October 17, 1975, and subsequently draft application guidelines were issued. Guidelines for conditional HSA designation in Minnesota were issued by the State Planning Agency, December 16, 1975. It was announced earlier that all "B" Agencies, singly or in combination, were applying for designation as HSA's. Public hearings on these applications were held in six of the seven health service areas in December, 1975, and January 1976.

The MSMA advised all county medical societies by letter and telephone of the sequence of these events prior to the public hearing in each area and again stressed the importance of physician participation in the formation of the HSA's. It has been discouraging that physician participation at the hearings was less than good in spite of this effort by the staff. How can we make our members understand how important it is for a physician to participate as corporate members and members of the Board of Directors of HSA's in the maximum numbers allowed by the guidelines and regulations of this Act?

Prior to and since the enactment of P.L.93-641 on January 4, 1975, medical spokesmen and leaders have, without exception, expressed the opinion that the Health Planning Act is the most important health legislation ever enacted with the potential of drastically altering the practice of medicine in the United States. Certainly, this possibility should stir even the most complacent and uninvolved in the medical profession to seek involvement and active participation in the HSA's. Even casual reading of the sections on National Guidelines and Priorities reveals that the priorities of action include: (1) the development of multi-institutional systems for coordination or consolidation of institutional health services (including obstetric, pediatric, emergency medical, intensive and coronary care, and radiation therapy services), (2) the development of medical group practices (especially those whose services are appropriately coordinated or integrated with institutional health services), health maintenance organizations, and other organized systems for the provision of health care, (3) the training and increased utilization of physician assistants, especially nurse clinicians and (4) the adoption of uniform cost accounting, simplified reimbursement, and utilization reporting systems and improved management procedures for health service institutions.

It is inconceivable that these and the other priorities charged to the HSA's can be considered and evaluated without a large measure of physician participation. As a matter of fact, it is recognized in the law that it is "imperative that the provider be encouraged to play an active role in developing health policy at all levels." This is an invitation to play an active role that we cannot ignore. It is time and even past time that every physician participate actively in health planning. What have *you* done and how are *you* planning to participate?

GR Diessner

G. Roy Diessner, M.D.
President
Minnesota State Medical Association

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Editor's Notebook

Warming Up Cold Statistics (Or: How To Talk To Floridians About Minnesota Winters)

"The coldest winter I ever spent was a summer in Duluth."—Mark Twain

Going to Florida this winter?

If a recent Florida experience of mine means anything, be prepared to answer questions about Minnesota weather. After the *Miami Herald* showed a wintry photograph of the 250 car pileup on 35W, Florida residents asked me these questions: How could such a thing happen? *What's it really like living* in that climate? How do you put up with it? Why don't you move to Florida?

As I groped for answers, I saw eyes bulge in disbelief. That is when I decided to write this editorial. What follows puts the cold facts of Minnesota winters in the best possible light. Perhaps you can use this series of conversational ploys for fending off Floridians who express morbid curiosity about Minnesota winters.

Discuss Distances

If a Florida resident tries to sympathize with you about the latest Arctic temperature recorded in International Falls, discuss distances.

Inform him International Falls lies 310 miles north of the Twin Cities. To judge Minnesota weather on the basis of International Falls' temperatures is patently ridiculous. To compare the Falls with the Cities is like comparing frost-prone Jacksonville to frost-free Miami, which incidently is 345 miles south of Jacksonville.

Emphasize Twin City Temperatures

When talking temperatures, use high temperatures recorded in the Twin Cities, rather than other Minnesota cities, Why? Simply because the Twin Cities, with their larger size, have the biggest "heat shield." This warms the air, making temperatures higher. In other words, Twin Cities' temperatures are the hottest you're going to get, so take advantage of them.

Think High and Hot

Always speak of high temperatures, never of lows.

Here, for example, are highest temperatures in the hottest years in Twin Cities' history during the winter months:

	November	December	January	February	March
Highest Temperature	77	63	59	61	83
In Hottest Year	1933	1939	1846	1896	1910

Never Quote Lows

Never, I repeat *never,* quote *lows:* the 41 below record in the Twin Cities or the 46 below record at International Falls. Don't point out that the average January low is actually *only* three *above* zero, or that *only* 40 percent of January days have a low below zero. This information may impress Minnesotans, but it only demoralizes Floridians. They won't believe the figures anyway.

Avoid Wind Chill Factor

Avoid discussing the Wind Chill Factor. Who cares how you define the Wind Chill Factor? Who wants to know a 20 mile an hour wind on a 20 degree day feels like nine below? Certainly not the Floridian. And not the Minnesotan on vacation either.

Therefore, for the comfort of all concerned, do not give out the formula for calculating the Wind Chill Factor, where V is the wind speed in meters per second and T is the air temperature in degrees Centigrade, and H is the temperature equivalent plus wind on exposed flesh:

$$H = (0.14 + 0.47\sqrt{V}) \times (36.5 + T)$$

The Florida resident already knows enough about exposed flesh.

Push Discomfort Index

Instead of discussing the Wind Chill Factor, push the Discomfort Index. The higher the heat and humidity, the greater the Index. You calculate the Index by adding wet-bulb and dry-bulb temperatures, multiplying by 0.4 and adding 15. A Discomfort Index over 75 is uncomfortable for most people; an Index over 80 is acutely uncomfortable for anybody. Up to 95 degrees there is discomfort at any humidity. At a temperature of 102 there is acute discomfort at any humidity. Since the Floridian won't remember the Discomfort Index formula or any of these figures, provide him with this chart so he can calculate his discomfort.

Discomfort Temp.-Humid.	Acute Discomfort Temp.-Humid.	Discomfort Temp.-Humid.	Acute Discomfort Temp.-Humid.	Discomfort Temp.-Humid.	Acute Discomfort Temp.-Humid.
75°—100%	81°—100%	82°—49%	88°—54%	90°—14%	96°—20%
76°— 91%	82°— 93%	83°—43%	89°—49%	91°—10%	97°—16%
77°— 82%	83°— 86%	84°—38%	90°—43%	92°— 7%	98°—13%
78°— 75%	84°— 78%	85°—33%	91°—38%	93°— 5%	99°—11%
79°— 68%	85°— 71%	86°—29%	92°—34%	94°— 3%	100°— 8%
80°— 61%	86°— 65%	87°—25%	93°—30%	95°— 1%	101°— 6%
81°— 55%	87°— 59%	88°—20%	94°—26%	96°— 1%	102°— 3%
		89°—17%	95°—23%	97°— 1%	103°— 1%

The foregoing has absolutely nothing to do with Minnesota weather, which is exactly the point. The Discomfort Index is a diverting maneuver.

Minnesota Has a "Dry Cold"

Minnesota has a "dry cold"—the kind you don't feel (unless you're outside, of course). Besides, the Mean Absolute Humidity (whatever that is) reaches its lowest point in the coldest months.

Month	Mean Absolute Humidity in Twin Cities (g/M³)
January	2.0
February	2.1
March	3.2
April	5.0
May	7.4
June	10.6

Florida, on the other hand, has a "wet heat"—the kind that drenches you with sweat and makes you intensely uncomfortable (and attracts Minnesotans in droves). I'm reminded of what a wise old Minnesota farmer, Andrew Cleland of Northfield, once said to me: "You can always put something on, but there's only so much you can take off."

Have Fun With the Sun

Suppose your listener is not impressed by your arguments up to this point.

(Continued on page 97)

adjunctive therapy for wound debridement

HELPS TO REMOVE:

- Necrotic Tissue and Associated Odor

HELPS PREPARE WOUND FOR:

- Granulation/Healing
- Granulation/Grafting

CLEANSE WOUND
Thoroughly cleanse and irrigate wound area with sodium chloride or water solutions. Wound MUST be cleansed of antiseptics or heavy-metal antibacterials.

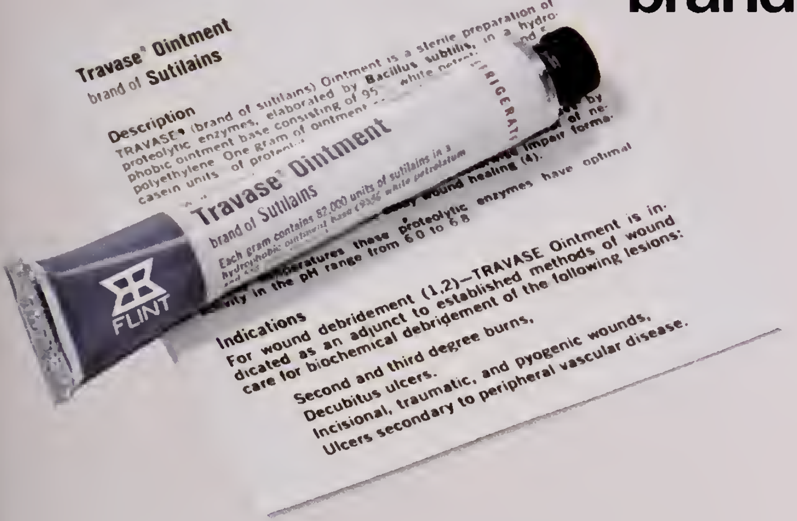
THOROUGHLY MOISTEN
Thoroughly moisten wound area either through tubbing, showering, or wet soaks (e.g., sodium chloride or water solutions).

APPLY ENZYME
Apply a layer of TRAVASE Ointment. Assure intimate contact with necrotic tissue and complete wound coverage.

APPLY MOIST DRESSING
Apply loose moist dressings (most important with dry leathery eschar).

CHANGE DRESSINGS
When changing dressing, gently wipe away the dissolved material. Repeat the procedure, including application of TRAVASE Ointment, 3 to 4 times per day for best results.

Travase® Ointment
brand of Sutilains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Description
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impair forma wound healing (4).
peratures these proteolytic enzymes have optimal activity in the pH range from 6.0 to 6.8

Indications
For wound debridement (1,2)—TRAVASE Ointment is indicated as an adjunct to established methods of wound care for biochemical debridement of the following lesions:

Second and third degree burns,
Decubitus ulcers,
Incisional, traumatic, and pyogenic wounds,
Ulcers secondary to peripheral vascular disease.

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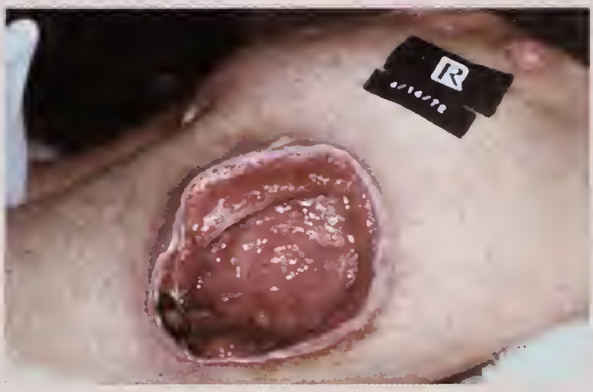
Please see next page for prescribing information.

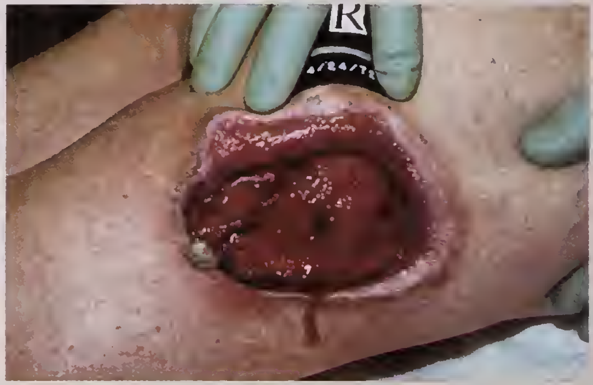
Travase® Ointment brand of Sutilains

ulcers

TERRY V. CARLE, M.D., CLINICAL INSTRUCTOR DEPT. OF PHYS. MED. & REHAB.,
CRAIG REHABILITATION HOSPITAL, UNIVERSITY OF COLORADO



Before treatment, necrotic matter coated the inner surfaces of this decubitus ulcer.



After six days of TRAVASE therapy, debridement is nearly complete and granulation evident.

burns

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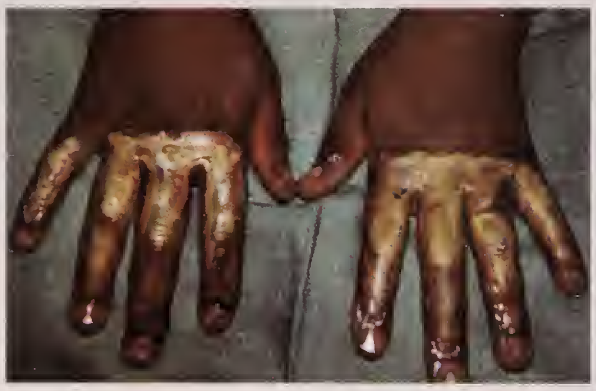
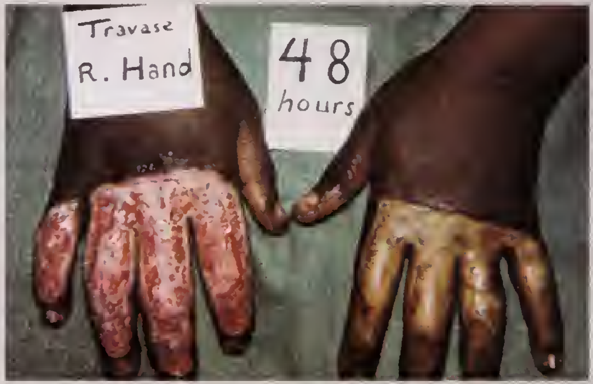


Before treatment . . .



48 hours following treatment with TRAVASE Ointment on right hand; left hand is control.

Travase® Ointment

(brand of Sutilains)

Indications: For wound debridement, TRAVASE Ointment is indicated as an adjunct to established methods of wound care for biochemical debridement of the following lesions:

- Second and third degree burns,
- Decubitus ulcers,
- Incisional, traumatic, and pyogenic wounds,
- Ulcers secondary to peripheral vascular disease.

Contraindications: Application of TRAVASE Ointment is contraindicated in the following conditions:

- Wounds communicating with major body cavities,
- Wounds containing exposed major nerves or nervous tissue,
- Fungating neoplastic ulcers,
- Wounds in women of child-bearing potential—because of lack of laboratory evidence of effects of TRAVASE upon the developing fetus.

Warning: Do not permit TRAVASE Ointment to come into contact with the eyes. If contact is made, immediately rinse with copious amounts of water, preferably sterile.

Precautions: A moist environment is essential to optimal activity of the enzyme. Enzyme activity may also be impaired by certain agents (see package insert). Although there have been no reports of systemic allergic reaction in humans, studies have shown that there may be an antibody response in humans to absorbed enzyme material.

Adverse Reactions: Consist of mild, transient pain, paresthesias, bleeding and transient dermatitis. Pain usually can be controlled by administration of mild analgesics. Side effects severe enough to warrant discontinuation of therapy occasionally have occurred.

If bleeding or dermatitis occurs as a result of the application of TRAVASE Ointment, therapy should be discontinued. No systemic toxicity has been observed as a result of the topical application of TRAVASE Ointment.

DOSAGE AND ADMINISTRATION: STRICT ADHERENCE TO THE FOLLOWING IS REQUIRED FOR EFFECTIVE RESULTS OF TREATMENT:

1. Thoroughly cleanse and irrigate wound area with sodium chloride or water solutions. Wound MUST be cleansed of antiseptics or heavy-metal antibacterials which may denature enzyme or alter substrate characteristics (e.g., hexachlorophene, silver nitrate, benzalkonium chloride, nitrofurazone, etc.).
2. Thoroughly moisten wound area either through tubbing, showering, or wet soaks (e.g. sodium chloride or water solutions).
3. Apply TRAVASE Ointment in a thin layer assuring intimate contact with necrotic tissue and complete wound coverage extending ¼ to ½ inch beyond the area to be debrided.
4. Apply loose wet dressings.
5. Repeat entire procedure 3 to 4 times per day for best results.

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Contents—February, 1976

Volume 59, 2
Pages 67-144

OVER PAINTING—“Mayo Medical School Student Center”
Harold H. Crawford ... 106

RESIDENT'S LETTER—Participation in Planning
G. Roy Diessner, M.D., President ... 71

DITOR'S NOTEBOOK—Warming Up Cold Statistics
Richard L. Reece, M.D., Editor-in-Chief ... 73

RIGINAL CONTRIBUTIONS

Intractable Ascites—A New Approach
James McMillen, M.D. et al. ... 79

Transverse Myelopathy Following the Use of Heroin
Myoung C. Lee, M.D. et al. ... 82

Two Primary Intracranial Tumors of Different Histological Type
Sidney K. Shapiro, M.D. et al. ... 84

Table Appliance for Use in Proctosigmoidoscopy
Harry B. Neel, M.D. ... 88

DITORIALS

Pre-Hospital Life Support as a Component of Emergency Medical Services
Roger D. White, M.D. ... 93

Focusing on the Cause of Sudden Infant Death Syndrome
Ralph A. Franciosi, M.D. ... 94

ETTER TO THE EDITOR—Duluth Water Revised
James R. Coleman ... 95

ERSPECTIVE—The Pelvic Examination—A View from the Other End of the Table
Joni Magee, M.D. ... 99

-RAY CONFERENCE—Large Pulmonary Nodules in a Young Man
Wm. A. Wilcox, M.D. and C. J. Swendseen, M.D. ... 105

INNESOTA STATE MEDICAL ASSOCIATION—Annual Meeting
R. D. Semsch, M.D. ... 107

LINICAL PATH CONFERENCE—Histoplasmosis in an Elderly Female
D. K. Ohrt, M.D. and Mary E. Paul, co-editors ... 113

PECIAL ARTICLE—Implementation of an Expanded Emergency System
Brian C. Campion, M.D. et al. ... 123

UR POLITICAL RESPONSIBILITIES AS PHYSICIANS
Mathias Masem ... 135

ONTINUING EDUCATION ... 87, 97, 137

LASSIFIED ADVERTISEMENTS ... 108

NDEX TO THE ADVERTISERS ... 144

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Intractable Ascites

A New Approach

JAMES McMILLEN, M.D.;* JOHN P. DELANEY, M.D., Ph.D.;† and
MICHAEL LEVITT, M.D.‡

A new treatment for intractable ascites, the placement of a valved plastic conduit between the peritoneal cavity and the subclavian vein, has recently been described by LeVeen.[1] A patient who experienced marked relief from otherwise intractable ascites is described.

THE STANDARD MEDICAL management of ascites consists of bedrest, fluid restriction, salt restriction, and the judicious use of diuretics. On this regimen, most patients will successfully mobilize the ascitic fluid. Occasionally, however, patients with intractable ascites respond to these non-mechanical attempts to remove ascitic fluid with reduction of the extracellular space and development of progressive oliguria.

If the abdominal distention is incapacitating, two alternatives to medical therapy are available. One is paracentesis, with or without intravenous reinfusion of the ascitic fluid, an effective short-term therapy but impractical for the long term. The second alternative is surgical construction of a portal-systemic venous anastomosis. Recently another operative approach, the placing of a plastic conduit between the peritoneal cavity and the subclavian vein, was introduced by LeVeen.[1] The present paper describes the course of a patient with intractable ascites who experienced marked improvement from the placement of such a peritoneal venous shunt.

Case Report

This 45-year-old white female had a history of heavy ethanol ingestion dating to her late teens. She was essentially free of any health problems until six months prior to this admission, at which time she developed nausea, vomiting, and right upper quadrant pain. The gallbladder was not visualized on an oral cholecystogram and a cholecystectomy was subsequently performed. Liver biopsy taken at operation showed changes compatible with alcoholic hepatitis and moderate cirrhosis. The gallbladder specimen had histologic changes of chronic cholecystitis but no stones. The immediate postoperative course was uncomplicated. However, in the ensuing weeks the patient developed progressive ascites with her weight increasing from 180 to 200 lbs. Liver function tests, including serum glutamic oxaloacetic transaminase, alkaline phosphatase, lactic dehydrogenase, and bilirubin, done during that time were within normal limits. Intensive medical therapy consisting of a 500 mgm sodium diet, fluid restriction, infusion of salt poor albumin and diuretics was begun. Nevertheless, the patient continued to gain weight, with progressive abdominal distention, and was transferred three months after cholecystectomy to the University of Minnesota Hospitals for further evaluation and treatment.

Vital signs on admission were: blood pressure 100/70, pulse 100 and regular, respirations 24, temperature 98.6, and weight 211 lbs.

Physical examination revealed a gaunt faced 45-year-old white female complaining of marked discomfort from abdominal distention. Abnormal findings included palmar erythema, spider telangiectasias, gross ascites, and 4+ pitting edema to both knees. Neither liver nor spleen enlargement was detectable and there was no jaundice.

Admission laboratory results included a hemoglobin of 12.2 and a hematocrit of 38 with normal erythrocyte indices. The leukocyte count was 9,000 with 83% neutrophils and seven lymphocytes. The platelet count was 250,000. The serum sodium was 114, potassium 3.5, chloride 80, and carbon dioxide 25 meq/liter. The urea nitrogen was 24 mgm% and the creatinine 1.2 mgm%. Liver function tests revealed slightly elevated alkaline phosphatase 204 I.U. (normal to 170). The serum glutamic oxaloacetic transaminase was 23 I.U., bilirubin 0.1 direct, 0.6 mgm% total, albumin 3.1 gm%, globulin 1.0 gm%, total protein 6.6 gm%. The cholesterol was 237 mgm%, the prothrombin time 12.9 seconds, and partial thromboplastin time 36.0 seconds. Serum and urine amylase values were initially elevated but returned within a day to normal. The urine had a specific gravity of 1.017, a pH of 7.0, 1+ protein, 1+ white blood cells. Urine culture grew 100,000 colonies of E. coli. Urinary electrolytes were Na—3 meq/liter and K—75 meq/liter; osmolality was 504. Stool guaiac was negative.

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Chest Xray was within normal limits except for basilar atelectasis. Xrays of the abdomen were negative except for ascites. The electrocardiogram was within normal limits. Skin testing with PPD was negative. Alpha-feto-protein was negative. Isotope scan showed mild enlargement of the liver and spleen and moderate decrease in hepatic uptake with no mass lesions.

Diagnostic paracentesis, done on the second hospital day, revealed a glucose of 113 mgm%, protein 4 gm%, amylase 132 Somogyi units, and a leukocyte count of 88 with predominantly mononuclear cells. Cytology was negative for malignant cells as were all cultures including aerobic, anaerobic, fungus, and TBC. Repeat paracentesis was performed on the fourth and eighth hospital days with the same results. Because of the high protein content of the peritoneal fluid, the diagnosis of hepatic vein occlusion or Budd-Chiari syndrome was considered. However, a venogram showed the vena cava and hepatic veins to be patent.

Further medical management aimed at reducing the volume of ascites was instituted. The regimen included a 500 mgm Na diet, fluid restriction to 1,000 cc, and Spironolactone 50 mgm four times a day by mouth. Her weight dropped five pounds by the fourth hospital day but then began to increase (Figure). Medical management was intensified by restricting dietary salt intake to 250 mgm per day and increasing the Spironolactone to 150 mgm three times a day. On this regimen, the patient became progressively more hypotensive and oliguric. The arterial blood pressure dropped to 75/40 and the urine volume fell to 200 cc per day with the BUN rising to 30 and the creatinine to 1.9.

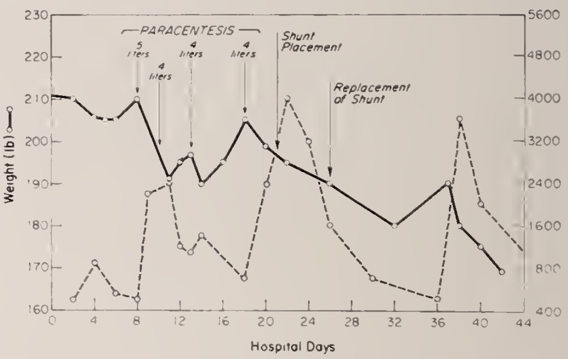
The patient became confused and appeared to be near death. On the eighth hospital day, five liters of peritoneal fluid were removed and infused intravenously through a blood filter apparatus at a rate of 100-150 cc/hour. The immediate response to this procedure was return of blood pressure to near normal and improvement in the mental status. The patient became comfortable and alert; the urine volume was 2,200 cc on the following day. Paracentesis on days eleven and thirteen coupled with reinfusion of the ascitic fluid maintained an adequate urine volume and the patient's weight dropped to 190 lbs.

Despite continued vigorous medical management, however, her weight had increased to 205 lbs. per day eighteen and she was once again markedly uncomfortable with respiratory distress. Because the urine volume was approaching oliguric levels, another five liters of ascitic fluid were removed on the eighteenth hospital day and reinfused. At this time we elected to insert a LeVeen peritoneal-venous shunt because the only measure which has successfully induced a diuresis had been intravenous infusion of ascitic fluid.

On the 21st hospital day the shunt was placed under local anesthesia, as described by LeVeen.[1] A small incision was made in the left upper quadrant down to the peritoneum. A purse string suture was placed and the multi perforated tube inserted through a tiny hole in the peritoneum. The tube was fixed with additional sutures to the posterior rectus sheath. The right internal jugular vein was exposed through a vertical incision. Local anesthetic was infused into the skin and subcutaneous tissue between the two incisions and a tunnel developed with long clamps up to and over the clavicle. The other end of the tube was pulled through the tunnel, threaded into the superior vena cava, and tied into the internal jugular vein.

The patient had an immediate diuresis of 4,000 cc during the next 24 hours. She was given Lasix, 40 mgm four times a day, and her weight progressively dropped to the level of 190 lbs. By the fifth postoperative day, however, the weight had appeared to stabilize and there was some concern that the shunt might have kinked or clotted. The neck incision was re-explored and the tube removed from the jugular. Ascitic fluid flowed freely from the tube, indicating no obstruction and it was replaced in the superior vena cava via the jugular vein.

During the subsequent three weeks the patient's weight gradually fell to 168 lbs at the time of discharge. She felt well, although there were several unexplained episodes of abdominal pain associated with nausea. Serum and urine amylase values were normal as was repeat diagnostic paracentesis. During the 32nd and 36th days, it was feared that the shunt might have ceased functioning because of weight increase to 190 lbs. This proved to be temporary and the patient again began spontaneous diuresis by the 40th hospital day.



Figure—Graphic Representation of Patient's Weight and Urine Volume Before and After Shunt Placement.

Before discharge, she was fitted with a tight abdominal binder and instructed on breathing maneuvers consisting of sucking air through a bottle which required a negative pressure of eight cm of water. These two measures are aimed at enhancing flow from the abdominal cavity to the thoracic cavity by amplifying the pressure gradient. The patient was discharged on Aldactone, 25 mgm three times a day. She was seen as an outpatient one month after discharge, at which time she felt well and her weight was recorded as 167 lbs.

Since discharge the patient has been regularly followed at University Hospitals. Her course was complicated by an episode of oliguria of undetermined etiology, that successfully responded to medical therapy. At that time shunt patency was documented by the direct injection of contrast material. Since then she has continued to do well with the most recent weight being 130 lbs.

Discussion

The patient described in this report represented a difficult diagnostic as well as therapeutic problem. Although the liver biopsy demonstrated rather typical alcoholic hepatitis and Laennec's cirrhosis, consistently high ascitic fluid protein of greater than 4 gm% is seldom observed in uncomplicated cirrhosis.[2,3] Three possible causes of ascites with a protein content are a leak of pancreatic juice into the peritoneal cavity (pancreatic ascites), occlusion of the hepatic veins, and infection. These three conditions were deemed very unlikely because of normal amylase levels in the ascitic fluid, patent hepatic veins on angiography, and negative cultures of the ascitic fluid. Thus, while atypical, the ascites appeared to be secondary to the cirrhotic process.

The ascites in this patient was not only resistant to vigorous medical therapy but actually became life threatening on several occasions with the development of hypotension, hypoventilation, oliguria, and confusion; all of which were promptly relieved by paracentesis. In studies of the hemodynamic alterations in cirrhosis, Cohn described a subgroup of patients with similar symptomatology.[4-6] These subjects tended to have high hepatic vascular resistance, poorly developed portal systemic shunting, and the rapid development of intractable ascites, hypotension, and oliguria. The high ascitic fluid pressure in this syndrome apparently compresses the inferior vena cava and compromises venous return to the heart, contributing to the subsequent development of hypotension and oliguria.

Several therapeutic alternatives are available to correct this abnormality. Paracentesis with reinfusion of the ascitic fluid results in dramatic but temporary improvement, as seen in our patient. This modality is not feasible for long-term management[7] and may have associated complications.[8-10] There have been numerous surgical maneuvers designed to increase absorption of the ascites and alleviate the portal hypertension[11-19] none of which have been received very enthusiastically. Decompression of the portal system by portal-systemic anastomosis has been the most rational form of operation.[20] This procedure, however, is associated with substantial operative morbidity and mortality and may result in hepatic encephalopathy and accelerated deterioration of liver function because it deprives the injured liver of needed portal inflow.[21]

Recently LeVeen[1] described an alternative surgical approach to the problem of intractable ascites in which a silastic catheter is used to shunt ascitic fluid from the peritoneal cavity to the superior vena cava. Such tubes have been tried previously without success because the valves employed permitted a small amount of blood to reflux into the venous end of the catheter. This inevitably led to obstruction by a clot. The tube designed by LeVeen has a one-way pressure activated valve which prevents blood from entering the tube. This catheter can be inserted under local anesthesia, which is particularly advantageous in patients with deranged liver function, who frequently have a poor tolerance for general anesthesia. Furthermore, the massive ascites tends to compromise ventilation during general anesthesia.

Flow through the shunt obviously depends on the pressure gradient between the peritoneal cavity and the vena cava. The rapid decrease in weight immediately following placement presumably reflected a rapid initial movement of fluid through the shunt with expansion of the vascular volume and resultant brisk diuresis. However, after the pressure was reduced in the peritoneal cavity, fluid movement apparently slowed as did urine output and rate of weight loss. In an attempt to maintain the pressure gradient, abdominal binders and sucking maneuvers are employed to increase intraperitoneal pressure and reduce intrathoracic pressure. Although this patient still retains some ascitic fluid, her present weight is about 70 lbs less than that which she maintained while on extremely vigorous medical treatment; she has no discomfort from abdominal distention. Our experience is in accord with results reported by LeVeen, et al., in which 28 of 37 patients with intractable ascites obtained marked and sustained reduction in ascites from placement of such a shunt.

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*Special thanks to Dr. Jay Cohn for critical review of this manuscript.

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Transverse Myelopathy Following the Use of Heroin

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In a case of severe transverse myelopathy following intravenous injection of heroin, a myelogram showed diffuse widening of the thoracic spinal cord with high grade but incomplete block between the fourth and seventh thoracic levels. A spinal angiogram was normal. The clinical course was most consistent with that of spinal cord infarction.

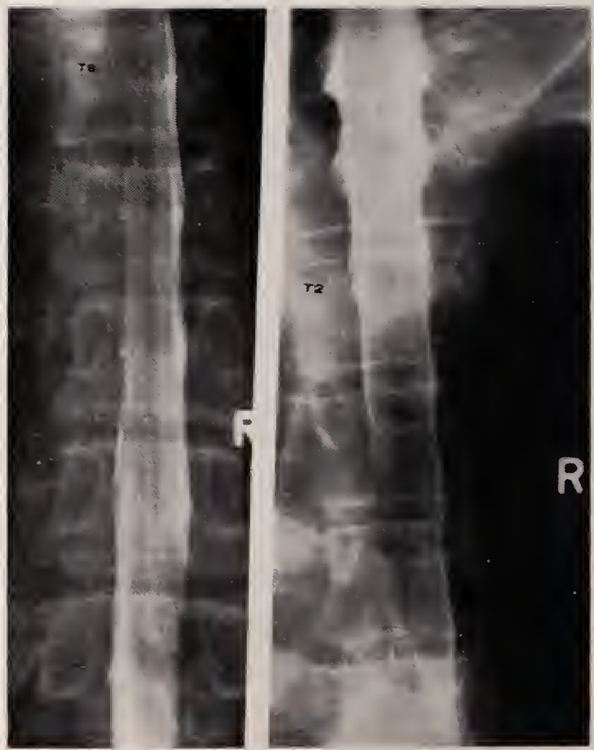
THE NEUROLOGIC MANIFESTATIONS associated with heroin abuse are protean and include coma with or without seizures, delirium, deafness, increased intracranial pressure, toxic amblyopia, peripheral neuropathy, myopathy and rhabdomyolysis.[1] Fifteen cases of transverse myelitis among heroin users have also been documented.[1-5] Myelography was performed in five of these cases, only one of which revealed a significant abnormality. The etiology of this rare neurologic complication among heroin users is unknown.

The patient described below developed a transverse myelopathic syndrome following an intravenous injection of heroin.

Case Report

The patient was a 22-year-old white male with juvenile diabetes mellitus being managed with a daily regimen of 44 units of NPH insulin, 18 units of regular insulin and an 1800 calorie diabetic diet. His diabetes was well-controlled. He allegedly began using heroin in 1970, with weekly intravenous injections. On December 8, 1973, he injected intravenously 0.1 gram white powdered heroin (about 50 mg.) after mixing with water. Within two to three minutes, he became slightly nauseated and then lost consciousness. He awoke approximately four to five hours later, confused and slightly dazed, but aware that he was unable to move his lower extremities. He was immediately taken to the local hospital where he was noted to be alert and well-oriented with a blood pressure of 90/64 and a regular pulse of 91 per minute. He was afebrile. The pupils were constricted bilaterally but responsive to light. The general physical examination was otherwise unremarkable. Neurologic examination revealed complete flaccid paraplegia. The deep tendon reflexes were normal in the upper extremities, but were absent to very hypoactive in both lower extremities. The Babinski sign was present bilaterally. Both pain and temperature sensations were severely reduced below the fifth or sixth thoracic sensory level, but light touch, vibration and position sensations were only moderately reduced.

An indwelling Foley catheter had to be placed. Cerebrospinal fluid examination disclosed only two leukocytes per cubic millimeter and an elevated protein of 610 mg%. For several days after admission, the patient was very agitated, restless, and tremulous, suggesting



Figure—Myelogram shows diffuse widening of the thoracic cord with a high grade but incomplete block between fourth and seventh thoracic levels.

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probable drug withdrawal. These symptoms were treated with hydration and sedatives. Blood pressure returned to normal shortly after admission. He subsequently presented a rather flat affect, but otherwise normal mental status. The patient was transferred to the University of Minnesota Hospitals on December 17, 1973.

The following laboratory studies were all normal: complete blood count, urinalysis, blood urea nitrogen, serum creatinine, serum electrolytes, VDRL, rheumatoid factor, L.E. clot test, fluorescent antinuclear antibody test, electrocardiogram, Xrays of the chest and spine, and electroencephalogram.

Myelography on December 19, 1973 revealed diffuse widening of the thoracic spinal cord with a high grade, but incomplete block between the fourth and seventh thoracic levels (see Figure). This was thought to represent severe spinal cord swelling. The cerebrospinal fluid obtained at the time of myelography showed a total protein of 150 mg%, with a gamma globulin fraction of 7.9%. There were 4 polymorphonuclear leukocytes and 19 monocytes per cubic millimeter. In an attempt to exclude the possibility of an arteriovenous malformation or vascular occlusion of the spinal cord, spinal cord angiography was performed. Selective catheterization of the radicular arteries of the spinal cord was carried out through the right femoral artery. No significant abnormalities were found. The artery of Adamkiewicz was well visualized and was normal throughout its course.

His diabetes remained under satisfactory control. At the time of discharge on January 11, 1974, he was severely paraparetic. Both lower extremities became gradually spastic. On follow-up examination approximately ten months later, a severe spastic paraparesis of both lower extremities with only minimal voluntary movements of the muscles was still present; there was moderate impairment of pain and temperature sensations below the sixth thoracic dermatomal level, but only mild impairment of vibration and position sense. The Babinski sign was still bilaterally present. His neurogenic bladder remained unchanged.

Discussion

The present case illustrates the salient characteristics of transverse myelopathy associated with heroin abuse. The clinical features in this patient are similar to those in 15 previously reported cases.[1-5] In other patients there has usually been a history of prior heroin use ranging from a single exposure[4] to many years of heavy narcotic use.[2] Although not present in this case, a period of abstinence from heroin use frequently antedated the onset of paralysis after heroin injection. Loss of consciousness shortly after heroin injection was also frequently reported.[2] Abnormalities of the cerebrospinal fluid were frequent and consisted of mild pleocytosis and elevated total cerebrospinal fluid protein.[1-4] The cerebrospinal fluid gamma globulin and serology have been invariably normal. Myelography was performed in five of 15 previously reported cases;[1-3] in one of these, focal widening of the cord was said to be present.[3] Unfortunately, the myelographic findings were not shown in the report. An apparently similar myelographic picture was present in our patient. The associated high grade block was undoubtedly related to the severe swelling in the involved segments of the thoracic spinal cord. The normal spinal cord vasculature demonstrated by angiography renders an arteriovenous malformation or a major vascular occlusion unlike to etiologic considerations in this patient.

In all such cases except for one,[4] the involvement was in the mid-thoracic spinal cord. In a case described by Schein,[4] the involvement was in the cervical cord.

The site of predilection for ischemic necrosis of the spinal cord is the mid-thoracic region, especially the fourth and fifth thoracic segments, presumably due to the relative paucity of vascular supply in this region. In the transverse section, the so-called watershed zone, primarily involving the pyramidal and spinothalamic tracts, appears to be most vulnerable to ischemia.[6] This pattern of involvement has been demonstrated in patients with spinal "stroke" due to severe hypotension.[7] Heroin commonly induces hypotension and respiratory depression. The present case was still hypotensive when he awoke after approximately four to five hours of unconsciousness. It is therefore reasonable to assume that severe hypotension and/or respiratory depression following heroin injection was directly related to spinal cord damage in this patient. Moreover, the clinical features and pattern of pathologic involvement in the present case are very similar to those described in patients with spinal "stroke." It seems probable that the present case, as well as the majority of reported cases of heroin-related transverse myelopathy, are due to temporary hypotension with resulting spinal cord infarction.

Other etiologic factors that may cause transverse myelopathy should be considered in this patient. These include demyelinating disease, infection, collagen vascular disease and neoplasm, However, the clinical manifestation of these various diseases is quite different. This patient did not have any other significant symptoms referable to any of these disorders prior to or following the onset of sudden paraplegia. Furthermore, myelographic findings make these etiologic possibilities unlikely.

The authors wish to thank Dr. A. B. Baker who provided valuable opinions in preparation of the manuscript.

References on page 87.

Two Primary Intracranial Tumors of Different Histological Type

Report of a Case with Both a Glioblastoma and a Meningioma

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and CHARLES A. HORWITZ, M.D.‡

A case report of a patient who was found to have at postmortem a meningioma and a glioblastoma multiforme in different hemispheres is presented. A review of the literature emphasizes the rarity of multiple primary intracranial tumors of different histological type in the absence of von Recklinghausen's disease. The difficulty of establishing the diagnosis antemortem is stressed.

THE OCCURRENCE OF MULTIPLE primary intracranial tumors of different histological types is of sufficient rarity to merit a case report. Courville[1] reported the incidence of multiple gliomas among intracranial tumors in general at 4.3%. He gave no figure as to the frequency of multiple primary intracranial tumors of different histological type. The preponderence of cases of multiple intracranial tumors is associated with von Recklinghausen's disease; in its absence, the incidence becomes low. Madonick et al.[2] surveyed the literature but failed to exclude the cases of von Recklinghausen's disease.

The following case report concerns a patient who had two primary intracranial tumors of different histological type in whom there was no evidence of von Recklinghausen's disease.

Case History

This 77-year-old female was admitted to Mt. Sinai Hospital, Minneapolis, Minnesota, on October 14, 1968. On the day before admission, she became disoriented, confused and lethargic and had a staggering gait. At the time of admission, she was found to be obese, extremely lethargic, and to have a blood pressure of 230/115. Mixed aphasia of both receptive and expressive type was evident. A right homonomous hemianopsia was demonstrated. A mild right central seventh nerve paresis was present. The patient had a rhythmic tremor plus mild cogwheel rigidity of the upper extremities. Romberg's sign was present and the gait was staggering. A detailed examination of the motor, sensory and coordination systems could not be performed because of the mental state of the patient. She was aphakic on the right. On fundoscopic examination, the patient had arteriovenous nicking. The remainder of the general physical and neurological examination was within normal limits. The patient had hypertension for 20 to 30 years. She also had a cardiac condition for some five years and used nitroglycerine on rare occasions.

Hospital Course

With bedrest alone, the blood pressure fell to normal. A mild glycosuria with elevated fasting and two hour postprandial blood sugars was noted. A diagnosis of diabetes mellitus was established, and the patient was placed on a diabetic diet and an oral hypoglycemic agent. Eight days after admission, the patient developed generalized clonic seizure activity. She was placed on diphenylhydantoin, and no further convulsions were noted.

An electroencephalogram seven days after admission was markedly abnormal with diffuse slow wave activity, most marked in the left temporal area. A lumbar puncture performed 16 days after admission disclosed a spinal fluid protein of 200 mg. percent. Xrays of the skull were normal with no shift of the pineal gland. The brain scan using 99MTc (Technetium) showed a large zone of abnormal isotope collection in the posterior aspect of the right parietal area as well as a more diffuse abnormality in the left temporal-parietal area from the temporal horn extending centrally almost to the midline. These isotope collections were considered to be consistent with multiple vascular accidents, metastatic neoplasm, or a combination of both.

Considerable technical difficulty was encountered in the performance of bilateral cerebral angiograms and in-

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complete filling was obtained. The question of angulation of the posterior parietal and angular branches of the middle cerebral artery on the right was raised. The patient's general condition gradually improved with partial clearing of the aphasia and progressive improvement in her ability to walk. Because of the possibility of metastatic carcinoma, upper GI series and barium enema were done and reported as unremarkable. The differential diagnosis at the time of her discharge, 23 days following admission, included: (1) multiple cerebrovascular accidents, (2) metastatic brain tumor.

The patient continued to improve at home for 11 days. There she developed weakness of the right arm and leg and became semi-comatose. The family at first refused rehospitalization but finally agreed 22 days after her initial discharge from hospital. At that time neurological examination revealed weakness in the right upper extremity and semi-coma. No papilledema was present. The family refused any further investigative procedures, and the patient died nine days after readmission to hospital.

Postmortem Findings

The brain weighed 1300 grams. There was a sharply circumscribed 4.5x3.5x3.5 cm. meningioma arising from the dura mater directly over the right cerebral hemisphere at the junction of the parietal and temporal lobes. The tumor was smooth, grey, and firm. There was a corresponding defect in the underlying cortex measuring 3.5x3.0x3.0 cm. An atherosclerotic vessel wound across the floor of the crater-like defect. A poorly defined capsule encased the tumor and separated it from the surrounding compressed cerebral cortex (Figure 1). Sections revealed a typical fibrous meningioma with bundles of interlacing spindly fibroblasts, focal hyalinization, and scattered psammoma bodies (Figure 2).

Sectioning of the fixed brain revealed a separate large friable multi-colored tumor (7x6x6 cm.) replacing the medial 60% of the left temporal lobe as well as portions of the left occipital and parietal lobes. At the level of the post-central gyrus there was replacement of much of the internal capsule and basal ganglia (Figure 3). Microscopically a typical "glioblastoma multiforme" (astrocytoma grade III) was characterized by astrocytic hyperplasia and anaplasia, prominent vascularity, astrocytic palisading about blood vessels, and occasional giant cell forms (Figure 4). The tumor was confined to the left cerebral hemisphere.

Brain stem, cerebellum, and right cerebral hemisphere were unremarkable. Moderate non-occlusive atherosclerosis was present in the Circle of Willis including the basilar artery and the smaller peripheral branches of the anterior and middle cerebral arteries, especially on the left side. No cerebral edema or signs of brain stem pressure were seen. Visceral examination showed: (1) bilateral pulmonary thrombo-emboli involving all lobes of the lung, (2) partial thrombotic occlusion of the right femoral vein, (3) focal acute bronchopneumonia with left lower lobe abscess formation, (4) a 0.5 cm. Hurthle cell

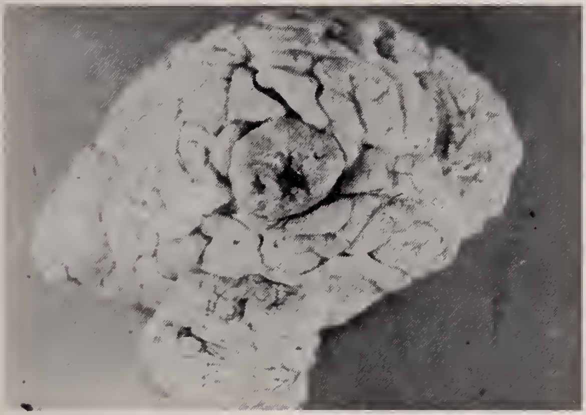

Figure 1.

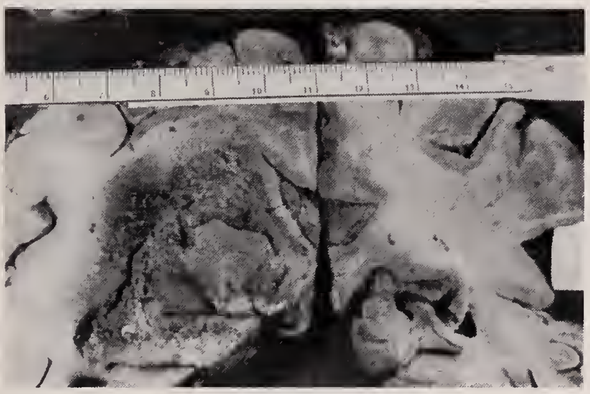

Figure 2.

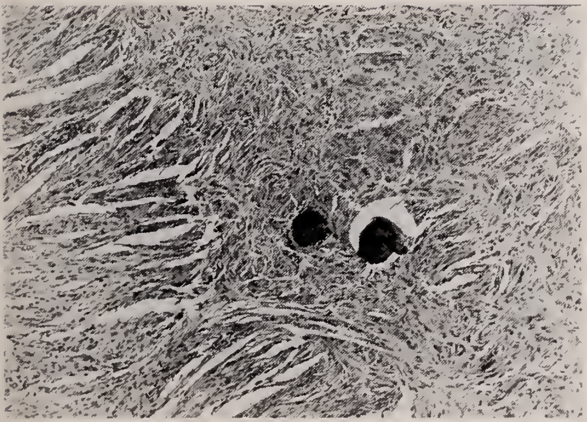

Figure 3.

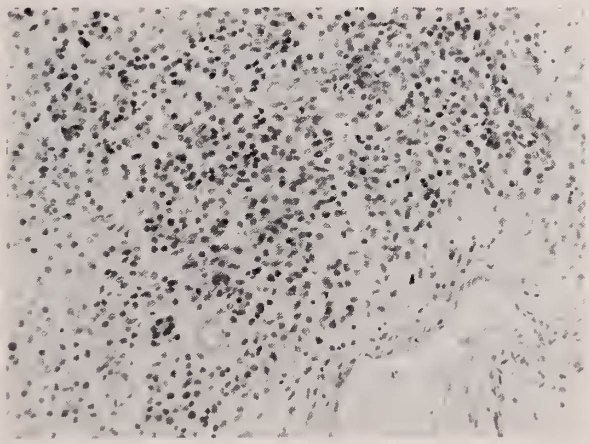

Figure 4.

adenoma of thyroid gland, (5) leiomyomata uteri, (6) diverticulosis coli, (7) exogenous obesity, (8) generalized arteriosclerosis, moderate.

Discussion

A modification of a survey presented by Madonick et al.[2] as indicated in the Table summarizes the literature with respect to two diverse primary brain tumors in the absence of von Recklinghausen's disease. In view of the rarity of this condition, it is not remarkable that with few exceptions, the diagnosis is established at autopsy. In several instances, one tumor was found by radiological studies or operation only to have the second tumor demonstrated at autopsy. The most frequent combination of tumors is meningioma and glioblastoma. This is not surprising as the former is the most frequent of the non-malignant and the latter is the most frequent of the malignant brain tumors.

The difficulty in establishing the antemortem diagnosis of multiple brain tumors is demonstrated by this case report.

This patient failed to show any shift of the pineal gland and the angiogram revealed no displacement from the midline. This finding of lack of shift of the midline structures is a diagnostic pitfall and tends to mitigate against the diagnosis of an intracranial tumor. A similar lack of displacement of midline structures is encountered in subdural hematomas which are bilateral and a possible explanation in each of these instances—namely, multiple brain tumors and bilateral subdural hematoma is that the pressure or volumetric changes are approximately equalized and the midline structures show no shift. The angiogram failed to establish the diagnosis and the brain scan was misinterpreted as possible metastatic carcinoma from multiple cerebrovascular accidents.

In several instances, the diagnosis of multiple tumors was established antemortem. Fiering and Davidoff's[3] patient had displacement of the right frontal horn of the lateral ventricle and a right frontal meningioma was removed. The pneumoencephalogram was then repeated and the left frontal glioblastoma located and operated upon. Angiography was of prime importance in establishing antemortem diagnosis in the case reported by Madonick et al.[2]

Conclusions

1. A patient with two primary brain tumors of different histological types in the absence of von Recklinghausen's disease is reported. 2. A glio-

TABLE

Multiple Diverse Primary Brain Tumors

Cases of Multiple Primary Brain Tumors Drawn from the Literature

Author	Types of Tumors	
		Plus
Austin, Barrows, and Grant[4]	Sarcomatous meningioma	Astroblastoma
Adam-Falkiewiczowa	Papilloma	Gliobastoma multiforme
Zulch	Meningioma (2 cases)	Monostrocellular sarcoma Pituitary adenoma
King and Botton	Meningioma	Spongioblastoma polare
Barla-Szabo	Meningioma	Glioma
Russell and Rubinstein[5]	Meningoma (5 cases)	Glioblastoma multiforme
Gass and Van Wagenen	Meningioma	Malignant oligodendroglioma
Fiering and Davidoff[3]	Meningioma	Glioblastoma multiforme
List, Williams, and Balyeat	Chromophobe adenoma	Glioblastoma multiforme
Love and Blackburn	Chromophobe adenoma	Meningioma
Wise, Malamud, and Boldrey	Chromophobe adenoma (2 cases)	Oligodendroglioma
Arieti	Meningioma (2 cases)	Astrocytoma
Alexander[6]	Meningioma	Spongioblastoma ependymale
Kirschbaum[7]	Meningioma	Subependymal glioblastoma multiforme
Myerson[8]	Meningiomas (2 cases)	Gliomas (4 cases)
Cushing and Eisenhardt	Meningioma	Glioblastoma
Hoffmann	Astrocytoma	Cerebellopontine angle meningioma
Brihaye, Danis, and Drochmans	Meningioma (optic nerve)	Glioma
Kessel	Meningioma	Acoustic neuroma
Fenyes and Kepes[9]	Meningioma (2 cases)	Glioma
Bartoloni	Glioblastoma	Meningioma
Tolentino and Giammusso	Glioblastoma multiforme	Meningioma

blastoma multiforme and a meningioma were encountered at post-mortem. These tumors are the two most frequently discovered in patients with diverse primary brain tumors.

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Annual Meeting
Minnesota Radiological Society

February 7, 1976

Sheraton-Ritz Hotel
Minneapolis, Minnesota

Scientific Program 1:00 p.m.

Business Meeting 4:00 p.m.

2nd Annual K. W. Stenstrom Memorial Lecture
8:00 p.m.
"Some Glimpses of a 20th Century Emigrant—K. W. Stenstrom"
Donn G. Mosser, M.D.

Table Appliance for Use in Proctosigmoidoscopy

HARRY B. NEEL, M.D.*

An appliance for improving patient comfort during proctosigmoidoscopy is described.

For performing proctosigmoidoscopic examination the knee-chest position is satisfactory. Although patients are instructed to support themselves on their extended arms, most of them "stand on their heads." If they maintain this position the examiner can observe and work with ease. Many patients have discomfort in the neck, become restless or slide to one side, and as a consequence, the examination is difficult for the physician and painful for the patient.

In order to improve patient comfort during proctosigmoidoscopy, the appliance shown in Figure 1 was constructed. It is placed on the examining table and rests on the head piece of the table. The shoulders of the patient lie against the well padded shoulder braces and the head is free in the compartment between the shoulder braces and the head piece of the table (Figure 2).

The use of the appliance has entirely eliminated head and neck pain during proctosigmoidoscopic examination. Position of the patient is easily maintained during the examination, and for more lengthy procedures such as biopsy, fulguration of polyps and minor operations on the anus. Patients who have had proctosigmoidoscopy with and without the use of this appliance, without exception, say that the appliance improves their comfort.

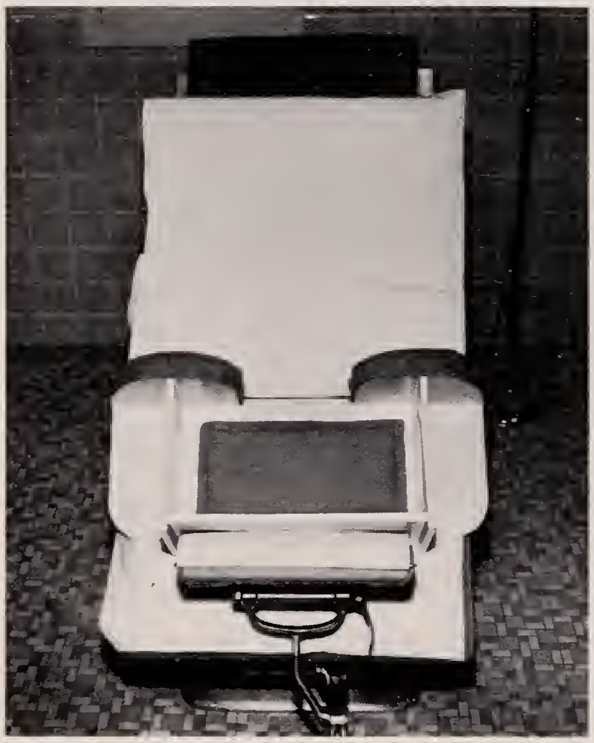

Figure 1—The appliance* rests on the head piece of the table which is in steep Trendelenburg position.

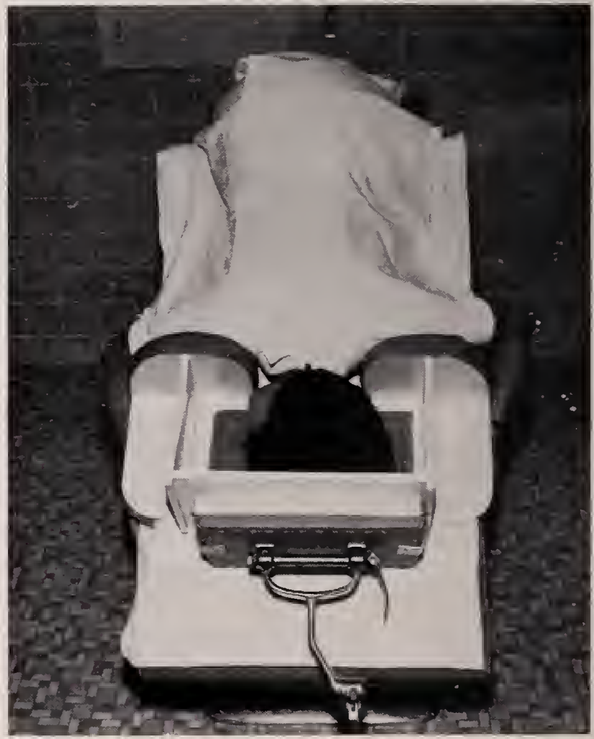

Figure 2—Patient in position for proctosigmoidoscopic examination. Shoulders rest on the well padded appliance. The head is free to move and there is no pressure on the head or neck.

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*Albert Lea, Minnesota.

*Made by Lyle McCoy, South Shore Drive, Albert Lea, Minnesota.

Natural balance
doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

ound useful in the management of vertigo* associated with ases affecting the vestibular system.

an relieve nausea and vomiting often associated with vertigo.*

Jsual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.

lso available as Antivert (meclizine HCl) 12.5 mg. scored ets, for dosage convenience and flexibility.

ntivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for sea, vomiting and dizziness associated with motion sickness.

F SUMMARY OF PRESCRIBING INFORMATION

NDICATIONS. Based on a review of this drug by the National Academy of iences—National Research Council and/or other information, FDA has classified e indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with otion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the stibular system.

Final classification of the less than effective indications requires further vestigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

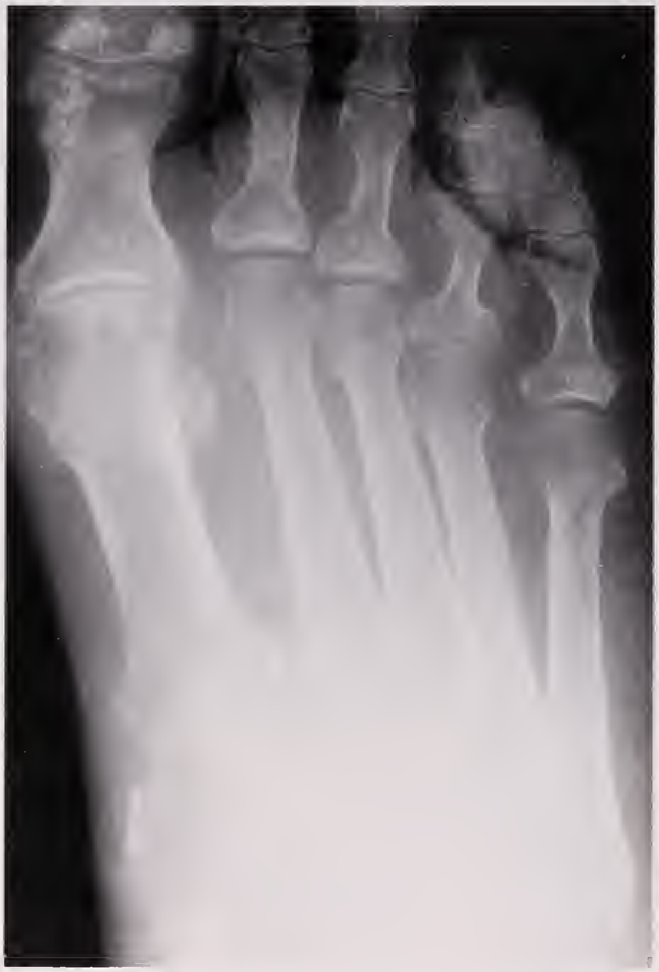
ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

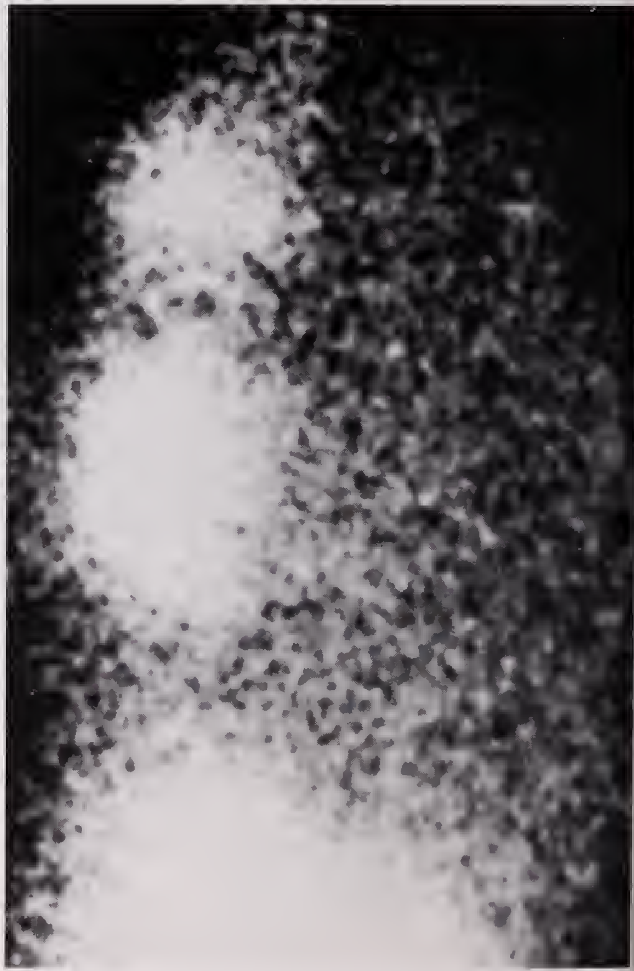
ROERIG Pfizer
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert®/25
(meclizine HCl) 25 mg. Tablets
# for vertigo*

VISUAL FOCUS ON ACUTE GOUTY ARTHRITIS



Foot of patient with acute gouty arthritis as seen by conventional x-ray.



Scintiphotogram of same foot reflects inflammatory process.

The scintiphotograph on the right shows increased uptake of radiotechnetium polyphosphate in the metatarsophalangeal joint and the proximal interphalangeal joint of the great toe of a patient with acute gou arthritis. This increased uptake probably results fro increased vascularity in the affected areas.

For a more detailed description of scintiphotography, see "addendum" at right.

THERAPEUTIC FOCUS
ON

CAPSULES, 25 mg and 50 mg

INDOCIN®

INDOMETHACIN | MSD)

*helps relieve pain
and other symptoms
of inflammation
in acute
gouty arthritis
in selected patients*

INDOCIN is a potent drug with anti-inflammatory, antipyretic, and analgesic properties. It should not be used in conditions other than those recommended. Although INDOCIN does not alter the progressive course of the underlying disease, in selected patients with acute gouty arthritis it has been found highly effective in relieving pain and in reducing fever, swelling, and tenderness.

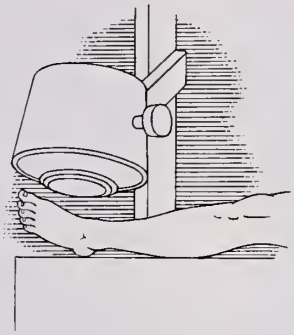
MSD
MERCK
SHARP&
DOHME

For a brief summary of prescribing information, please see following page.

MSD
MERCK
SHARP&
DOHME

addendum

Facts about Scintiphotography



In recent years a variety of radiopharmaceuticals have been employed to aid in the diagnosis of bone and joint disorders. The joint-imaging technique consists of injecting technetium polyphosphate intravenously, and imaging is performed with the scintillation camera two hours after the administration of the radionuclide. In general, for joint surveying, the shoulders, elbows, hands, wrists, knees, ankles, feet, and vertebral column are mapped. The entire scanning process takes approximately one hour. The criterion for a positive image is a higher concentration of radioactivity in a joint region than in adjacent nonarticular bone. In effect, each patient serves as his own control.

INDOCIN®
(INDOMETHACIN | MSD)

helps relieve pain
and other symptoms
of inflammation
in acute
gouty arthritis
in selected patients

**IMPORTANT NOTE: INDOCIN (Indomethacin, MSD) cannot be considere
a simple analgesic and should not be used in conditions other than thos
recommended. The drug should not be prescribed for children becaus
safe conditions for use have not been established.**

Because of the high potency of the drug and the variability of its potentia
to cause adverse reactions, the following are strongly recommended
1) the lowest possible effective dose for the individual patient should b
prescribed. Increased dosage tends to increase adverse effects, partic
ularly in doses over 150-200 mg per day, without corresponding clinic
benefits; 2) careful instructions to, and observations of, the individu
patient are essential to the prevention of serious and irreversible, in
cluding fatal, adverse reactions, especially in the aging patient.

Contraindications: Children 14 years of age and under; pregnant wome
and nursing mothers; active gastrointestinal lesions or history of recurren
gastrointestinal lesions; allergy to aspirin or indomethacin.

Warnings: *Gastrointestinal Effects:* Because of the occurrence and,
times, severity of gastrointestinal reactions, be continuously alert for an
sign or symptom signaling a possible gastrointestinal reaction. The risk
of continuing therapy with INDOCIN in the face of such symptoms mus
be weighed against the possible benefits to the individual patient. Gastr
intestinal effects may be reduced by giving the drug immediately afte
meals, with food, or with antacids. Use greater care in aging patients.

Ocular Effects: Corneal deposits and retinal disturbances, including thos
of the macula, have been observed in some patients on prolonged therap
Discontinue therapy if such changes are observed. Ophthalmologic exam
ination at periodic intervals is desirable in patients on prolonged therap

Central Nervous System Effects: INDOCIN may aggravate psychiatri
disturbances, epilepsy, and parkinsonism, and should be used with co
siderable caution in patients with these conditions. If severe CNS advers
reactions develop, discontinue the drug.

Precautions: Blurred vision may be a significant symptom that warrants
thorough ophthalmologic examination. Patients should be cautioned abo
engaging in activities requiring mental alertness and motor coordinatio
as driving a car. Headache which persists despite dosage reduction r
quires complete cessation of the drug. May mask the usual signs an
symptoms of infection; therefore, the physician must be continually o
the alert for this and should use the drug with extra care in the presenc
of existing controlled infection. After the acute phase of the disease
under control, an attempt to reduce the daily dose should be made r
peatedly until the patient is off entirely.

Adverse Reactions: *Gastrointestinal Reactions:* Single or multiple ulcer
tions of the esophagus, stomach, duodenum, or small intestine, includi
perforation and hemorrhage, with fatalities in some instances; rarely, inte
tinal ulceration has been associated with stenosis and obstruction; gastr
intestinal bleeding without obvious ulcer formation; perforation of pr
existing sigmoid lesions (diverticulum, carcinoma, etc.); rarely, increase
abdominal pain in ulcerative colitis patients or development of ulcerati
colitis and regional ileitis; gastritis, which may persist after the cessati
of the drug; nausea, vomiting, anorexia, epigastric distress, abdomin
pain, and diarrhea.

Eye Reactions: Corneal deposits and retinal disturbances, including thos
of the macula, have been observed on prolonged therapy; blurring
vision.

Hepatic Reactions: Rarely, toxic hepatitis and jaundice, including so
fatal cases.

Hematologic Reactions: Aplastic anemia, hemolytic anemia, bone marr
depression, agranulocytosis, leukopenia, and thrombocytopenic purpur
Since some patients manifest anemia secondary to obvious or occult ga
trointestinal bleeding, appropriate blood determinations are recommende

Hypersensitivity Reactions: Acute respiratory distress, including dyspn
and asthma; angiitis; pruritus; urticaria; angioedema; skin rashes; purpur

Ear Reactions: Hearing disturbances, deafness, tinnitus.

Central Nervous System Reactions: Psychic disturbances including ps
chotic episodes, depersonalization, depression, and mental confusio
coma; convulsions; peripheral neuropathy; drowsiness; lightheadedne
dizziness; syncope; headache.

Cardiovascular-Renal Reactions: Edema, elevation of blood pressur
hematuria.

Dermatologic Reactions: Loss of hair, erythema nodosum.

Miscellaneous: Rarely, vaginal bleeding, hyperglycemia, glycosuria, ulc
ative stomatitis, and epistaxis.

Note: In patients receiving probenecid, plasma levels of indomethacin a
likely to be increased.

Supplied: Capsules containing 25 mg indomethacin each, in single-u
packages of 100 and bottles of 100 and 1000; capsules contain
50 mg indomethacin each, in single-unit packages of 100 and bott
of 100.

*For more detailed information, consult your MSD representative or s
full prescribing information. Merck Sharp & Dohme, Division of Mer
& Co., Inc., West Point, Pa. 19486*

MS
MERC
SHAR
DOHN

Editorials

Pre-Hospital Life Support as a Component of Emergency Medical Services

SOME 650,000 PERSONS die annually in the United States secondary to acute complications of coronary artery disease. About 60% of these deaths occur outside the hospital—the pre-hospital phase of acute cardiac emergencies. While acute myocardial infarction is the usual cause of sudden episodes of ventricular fibrillation in such circumstances, many such deaths appear to be secondary to ventricular fibrillation without infarction; in such cases the fibrillation is apparently precipitated by an ischemic episode. In addition, such deaths are frequently very untimely, occurring in relatively young, previously healthy and gainfully employed persons. Such circumstances surely justify an aggressive approach in an attempt to deal with this kind of medical crisis.

It is recognized by all involved in the management of such situations that this is not the definitive answer to the problem; coronary artery disease with its complications is a major health problem necessitating intervention at the preventive level. Until that becomes a reality, we are left with the necessity to intervene vigorously when such a complication as ventricular fibrillation leads to collapse on the street, in the restaurant, in the football stadium, or at home.

Furthermore, unless aggressive advanced cardiac life support is applied at the scene and the victim of cardiopulmonary arrest stabilized there, the chance of survival is small indeed. With such an advanced system, about 15% of victims of pre-hospital ventricular fibrillation can be salvaged to long-term survival. In Seattle, Washington, where widespread citizen training in basic life support (cardiopulmonary resuscitation) has been undertaken, and where rapid system entry is available via a 911 telephone number and centralized dispatch, advanced life support at the scene has produced survival as high as 23%. It seems unlikely that this survival rate will be achieved on any widespread basis because it reflects a combination of nearly ideal circumstances not easily duplicated.

Campion et al.* describe in this issue the implementation of an advanced life support system operated by the St. Paul Fire Department in conjunction with St. Paul-Ramsey Hospital. Several points deserve comment. One has to do with the training program for the emergency medical technician-advanced (paramedic). There is as yet no consensus of opinion as to what is necessary or ideal in terms of content or length of training. In fact, too much emphasis has been placed on the length of training, in numbers of hours. Content needs to be defined, and programs characterized by what skills are taught and acquired, not how much time the student spends in a program. Fortunately, such an approach is currently under contract for evaluation, having been developed by the National Registry of Emergency Medical Technicians. When available, probably next year, this should facilitate a nationally standardized mechanism for paramedic training with built-in flexibility in accordance with local objectives, needs and capabilities.

Another important consideration has to do with the extent of capability of the paramedic. Ideally he should be trained to a level which permits him to manage a wide variety of emergencies, non-cardiac as well as cardiac. This capability is present in the St. Paul system, as the authors point out. In order to make this practical, however, the advanced training program may have to be modular in concept and function, so that different localities can gradually build up a service that meets their needs and yet can be progressively acquired using available resources.

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*See page 123.

One of the major objectives of advanced life support programs is to intervene in the patient's acute illness as early as possible. For example, in the patient with electrical instability accompanying acute myocardial infarction, it is obviously ideal to suppress potentially life-threatening ventricular dysrhythmias before they degenerate into ventricular fibrillation and cardiorespiratory arrest. This preventive aspect of pre-hospital life support, though more difficult to quantitate than the percentage long-term salvages from cardiac arrest, needs to be underscored as a major potential contribution of such systems.

Campion et al. quite candidly point out some of the problems with such a program, and there are often many others. Nevertheless, as their excellent paper indicates, such a system can become a reality when cooperation among participating agencies is achieved, existing resources fully utilized and additional needs defined and fulfilled. Program planners should look closely at the superb program developed by Campion and colleagues in St. Paul.

Roger D. White, M.D.*
Rochester, Minnesota

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*Assistant Professor in Anesthesiology, Mayo Medical School, and Consultant in Anesthesiology, (Cardiovascular), Mayo Clinic.

Focusing on the Cause of Sudden Infant Death Syndrome

SUDDEN INFANT DEATH Syndrome (S.I.D.S.) defines a sudden, unexpected death in an infant less than one year of age in which no apparent explanation of death is found after autopsy. The term is useful in documenting these cases and is helpful to parents experiencing S.I.D.S.[1] Death is precipitated by hypoxia as the final common pathway, but the trigger for hypoxia is unknown.[2]

S.I.D.S. causes 8,000-10,000 deaths per year in the United States. Epidemiological studies[3,4] repeatedly show that 90% of infants die before six months of age and 99% die during sleep. Death is not associated with an outcry.[5] The frequency of S.I.D.S. is higher in low income groups and infants born prematurely (less than 37 weeks gestation) or of low birth weight (less than 2500 gm.). Approximately 40% of S.I.D.S. cases have a "cold" several days prior to death.

Postmortem examination shows petechiae on the pleura, thymus, epicardium and lungs in 85% of cases.[2] There is pulmonary edema and visceral congestion. Microscopic examination shows focal infiltrates of lymphocytes and plasma cells in the larynx.

An explanation of death must be consistent with epidemiological and anatomical data. Interference with air intake through the upper airway correlates with these data.[6] A complex of factors can alter air intake e.g. obligate nose breathing,[7] mucosal edema, viscosity of nasal and epipharyngeal secretions, size of adenoids and tonsils and posterior displacement of the soft palate.[8] Perception of oxygen by nasal chemoreceptors, transfer of this information to the brainstem and the influence of brainstem output on respiration, apparently relate to the final common pathway of hypoxia.

Hopefully by focusing our attention on the upper airway, this hypothesis can be tested. This will require a combined anatomic and physiologic approach by multiple disciplines. The ultimate goal will be to define a group at risk for developing S.I.D.S. Then this group can be evaluated to determine if S.I.D.S. is preventable.

RALPH A. FRANCIOSI, M.D.*
Minneapolis, Minnesota

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*Children's Health Center, Minneapolis.

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Letter to the Editor

Dear Editors:

Duluth Water Revised

I read with interest the article by Arthur H. Wells, M.D., on Asbestos in Duluth Water (MINNESOTA MEDICINE, June 1975).* In some aspects this article may be misleading and, therefore, I offer the following comments on its content.

In the section entitled "Duluth Tap Water," the statement has been made that "Duluth ranges from 20 to 70 million fibers per liter by electron microscopy." The data made available by the Environmental Protection Agency (EPA), to the Courts, the Governor's Office and State agencies are lower than Dr. Wells indicates by about a factor of 10. The reported levels range from about 1 to 10 million fibers per liter. This was stated in a letter to Governor Anderson dated February 12, 1974, from Mr. Russell W. Peterson, Chairman of the Federal Council on Environmental Quality (CEQ), and this general level (1 to 10 million fibers per liter) was verified in a January 8, 1975, memo (from the Chief of the EPA Water Supply Program Support Activities to the Regional Water Supply Representative's EPA Headquarters). This memo provided the results of EPA analyses that had been reported at the second annual water quality technology conference in Dallas. The level for Duluth, Minnesota, was given as 1.1 to 4.8 million fibers per liter. Further, in the review by the U. S. Court of Appeals for the Eighth Circuit filed March 14, 1975, the level of fibers was stated to be approximately 12.5 million fibers per liter for *all* amphibole fibers, of which only 10 to 30 percent were consistent with amosite. Thus it would appear that the value stated (20 to 70 million fibers per liter) by Dr. Wells is a significant overstatement of the levels of exposure posed by the Duluth water supply. The result of this is to magnify the Duluth exposure calculated in the section on mathematics of a potential hazard by about a factor of 10.

In the paragraphs on the mathematics of potential hazard some additional comments are necessary. The first estimate is attributed to Dr. William J. Nicholson. As indicated above, since the fiber concentration is high by about a factor of 10 (about $5x10^6$ fibers per liter instead of $5x10^7$) the fibers ingested are also overestimated by a factor of approximately 10. Thus, using a more appropriate estimate of concentration the comparison would be 170 years of exposure as opposed to the 17 years of exposure shown.

The Appeals Court raised other questions about such calculations (these calculations are similar to, but not exactly like, those provided by Dr. Nicholson to the Court). It is informative to read what the Court of Appeals commented in this regard:

> "To make this calculation, Dr. Nicholson computed what he believed to be the level of exposure in a typical occupational environment and multiplied this figure by the total amount of air inhaled by the worker over a four year period (taken to be the relevant period in which a risk of excess gastrointestinal cancer was posed), thereby obtaining total fibers inhaled. A percentage reduction was then applied to obtain the number of fibers brought up the respiratory tract and swallowed. For Duluth residents, Dr. Nicholson calculated the number of fibers ingested over an 18 year period, assuming a daily intake of two liters of water and a fiber concentration of 25 million fibers/liter. From these assumptions, Dr. Nicholson opined that a Duluth resident over a period of 18 years ingested about two thirds of the amount of asbestos fibers swallowed by an asbestos worker in four years. As is evident, this calculation is beset by several uncertainties. The assumptions as to fiber concentration in occupational settings and the resulting percentage of fibers ingested involve margins of error. Furthermore, in assuming that the relevant fiber concentration in Duluth water was 25 million fibers/liter, Dr. Nicholson used a figure twice that found by the Court as the mean concentration of *all* amphibole fibers.[48,49] Reserve witness Dr. Gross performed a calculation similar to Dr. Nicholson's but using somewhat different assumptions, and concluded that Duluth water would have to contain several hundred million fibers/liter and be ingested for 60 years before an exposure comparable with occupational levels would be reached."
>
> ---
>
> "[48]As with the air counts, the water counts apparently include all types of amphiboles, only some of which are consistent with amosite asbestos. Thus, for example, Reserve witness Dr. Champness testified that samples of water taken from Two Harbors, Duluth, and Reserve's density

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*See page 458.

> current showed that the number of amphibole fibers with roughly the chemistry of amosite ranged from 13 to 34 percent. (A. 19:15) Plaintiffs' witness Dr. Langer testified that 47 percent of the fibers present in Duluth tap water were cummingtonitegrunerite and 8-9 percent of these fibers were in turn consistent with amosite. (A. 9:314-315)."
>
> "[49]The Court finds, consistent with the Court's study of amphibole fiber concentrations in the water supplies of Beaver Bay, Two Harbors and Duluth, that on the 28th of August, 1973, in the samples analyzed by seven laboratories that the mean fiber concentrations were: 12.5 million fibers per liter in the public water system at Duluth***." 380 F. Supp. At 48.

It is clear that the Nicholson comparison and the comparison made by Dr. Wells are far from exact and certainly appear to overstate the problem.

In the paragraph following the Nicholson calculation, Dr. Wells made some additional calculations based on the British standard of two fibers per cubic centimeter. It must be pointed out that this standard is related to the number of fibers greater than five microns in length only, and it appears that Dr. Wells has overlooked this fact.

For a general background we should recognize that all sampling of asbestos-type materials leads to the collection of a broad distribution of fiber sizes ranging from the very small sub-micron fibers on up to the larger fibers in multi-micron lengths. In the past it has been the general procedure to characterize the health importance of a concentration of such size distributed fibers in air by considering the number of fibers only in the size range greater than five microns in length. This is not to imply that only the fibers greater than five microns are important or that smaller fibers are not present, but only that the biological importance of the total distribution could be characterized by the group of fibers greater than five microns in length.

From the information that we have on air samples in the Silver Bay area and from information developed in the literature (The Interrelationships of Selected Asbestos Exposure Indices—J. R. Linch, et al., American Industrial Hygiene Association Journal, September-October 1970) we can estimate that on the order of a few percent of the total fibers in a characteristic distribution would be greater than the five micron length.

Thus, for comparison one must either multiply the standard by about 100 (to adjust for the total fiber distribution) or divide the total fiber counts by 100 (to adjust for the small fraction of fibers estimated to be greater than five microns in length). In any event, the calculations made by Dr. Wells would appear to overestimate the comparable intake by at least a factor of 1000 (100 on fiber size, 10 on fiber concentration).

In the concluding paragraph, Dr. Wells makes mention of the levels of asbestos observed in other environmental situations. It is informative to the reader to review some of these observations. The following information has been summarized from the open literature and/or the U. S. EPA's fiber studies.

Sample	**Approximate Range of Asbestos Fiber Concentration (millions of fibers per liter or kilogram)**
Duluth, MN	1.1 to 4.8
Jackson, MS	0.25 to 0.7
N. Troy, VT	0.98 to 2.2
San Francisco, CA	4.8
Newport, RI	0.4 to 1.0
Savannah, GA	1.74 to 2.03
Wilmington, DE	0.29
Tuscaloosa, AL	0.45
Municipal tap waters in Ontario, Canada; excluding Thetford Mines (27 supplies)	0.1 to 10
Thetford Mines Eastern Townships Quebec	178
Melted Snow Ottawa, Canada	34
Beer (4 types)	1 to 7
Wine (6 types)	2 to 12
Soft Drinks (4 types)	2 to 12
Japanese Rice	4000

As can be seen, the levels in the above selected water supplies and all beverages are in the same general range and not dissimilar to Duluth (with the exception of Thetford Mines which is significantly higher). The Canadian data include treated surface water supplies obtained from the Great Lakes of Superior, Huron and Ontario; and the St. Lawrence, Niagara and Detroit Rivers, all of which sources are also U.S. raw water supplies. For one raw water supply (the Detroit River at Windsor), the level of asbestos fibers reported by the Canadians for two samples was 18 and 25 million fibers per liter. It is obvious that the situation in Duluth is not greatly out of line with other observations in North America, and one might question why the water supply of Duluth and the State of Minnesota have been singled out for special interest by the EPA.

In closing, I would like to quote Mr. Garnet Kay of the Ontario Ministry of the Environment:

> "Apparently, there is asbestos in all surface waters of all inhabited areas of Ontario; and perhaps there has always been some asbestos there. We have only just discovered its presence as we will continue to discover new constituents therein."

James R. Coleman
Certified Health Physicist
Minneapolis, Minnesota

Editor's Notebook

(Continued from page 74)

What then?

Well, you might talk about the *Sunshine Quotient*. This *Quotient* proves that Minnesota—not Florida—deserves the title of Sunshine State (if you use Snow Glare Intensity in calculating the *Quotient*). Remind your listener that sunglasses are an absolute necessity to protect against the blinding glare of Minnesota winters. Then clinch your case by showing this Table of the *Sunshine Quotient* of the Twin Cities compared to Florida cities.

Sunshine Quotient **(% of Possible Sunshine + Number of Clear Days + Snow Glare Intensity) for Twin Cities versus Selected Florida cities.**

City	% of Possible Sunshine	Number of Clear Days	Snow Glare Intensity	Sunshine Quotient
Twin Cities	58%	98	100	256
Jacksonville	61%	99	0	160
Tampa	66%	98	0	164
Key West	73%	100	0	173

Note the Twin Cities have nearly as much sun as the Florida Cities. If you throw in Snow Glare Intensity, the Twin Cities win hands down.

Play the Name Game

Because Florida citizens may fail to get the notion of the *Sunshine Quotient,* you may want to play the name game. The idea behind the game is simple: Not everything is warm about Florida; not everything is cold about Minnesota.

Take, for example, surnames in the Miami and Twin Cities telephone directories. The greater Miami directory reveals 62 Winters, nine Shivers, six Colds, one Ice, 37 Snows, two Snowballs, 15 Blizzards, 45 Frosts, and one Freeze. At the other pole, the Minneapolis-St. Paul directories show 46 Summers, four Springs, two Hotts, one Heater, 74 Beaches, two Warms, two Warmings, one Sunn, 59 Sands, 10 Sweats, and 129 Palms.

These are the cold facts.

Richard L Reece MD

Continuing Education

Pediatric Day Sponsored by the Mayo Clinic

Pediatric Day sponsored by the Mayo Clinic will be held March 12, 1976. The Amberg-Helmholz Lecture, a feature of Pediatric Day, will be given by Barbara M. Korsch, M.D., of the Children's Hospital of Los Angeles. Presentations dealing with problems which occur in the practice of Pediatrics will be made by members of the staff of the Mayo Clinic. For information, write Doctor E. Omer Burgert, Program Director, Mayo Clinic, Rochester, Minnesota 55901.

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Perspective

The Pelvic Examination

A View from the Other End of the Table

JONI MAGEE, M.D.[*]

Lying on the examining table, feet in stirrups, confronting the examiner with the most personal parts of your anatomy, gives you plenty of time to think. Because I also perform pelvic examinations, what I thought about was what could be done to make me like them better. During the years certain parts of the procedure stood out as crucial. Speculum insertion is usually the most traumatic event in the examination. A detailed explanation of the sensations experienced and suggestions for alleviating some of them is presented. Other aspects of the doctor-patient relation during the pelvic examination are explored and suggestions for improving patients' perceptions of them are offered.

ONE PIECE OF ADVICE I heard in medical school that I'll never forget came from the chief of surgery: every surgeon should have a laparotomy once a year. His opinion, clearly, was that nothing improves doctor-patient rapport more than shared experience. During my myriad of pelvic examinations, instead of just looking at the ceiling, I thought a lot about why I didn't like most of them. After I became a resident in obstetrics and gynecology and was doing them myself, I got to understand exactly what the examiner was doing, and started to think about what would make the whole business less unpleasant. What follows is the result of what started as my supine ruminations.

Once upon a time I was referred to the office of a world-renowned specialist for investigation of a problem with great emotional impact for me. My history was taken by one of the lesser lights, but the pelvic examination was to be done by the chief himself. I was taken to the examination room and positioned and draped in the usual manner, legs in stirrups, sheet over my knees so I couldn't see past them, my perineum exposed to whatever breeze might have been stirring. The great man entered the room, followed by two associates, and walked to the head of the table. There, towering above me, he extended his hand and introduced himself. I had a powerful urge to laugh hysterically, curse him, and kick him, but I smiled sweetly and said "How do you do?"

Now, as they say on *Sesame Street,* "What's wrong with this picture?" Why did I react so violently? It took me years to figure out that the reason was that a handshake and an introduction imply a meeting between equals. However, that postural relation, with me in that very undignified, ludicrous, but necessary position clearly implied that I was helpless; nowhere near equal. The whole scene was so ridiculous and demeaning that it was an extremely unpleasant experience. The moral of the story is that if you have arrived to do a pelvic examination, introduce yourself to your patient while she is still sitting up, preferably clothed, but, anyway, sitting up. It doesn't take very long for her to lie down, and she'll feel much more human and happy.

Then, there she is and there you are, sitting down there between her legs where she can't see you, getting ready to apply all sorts of unknown tortures. What do you do? Hum a little tune? Many examiners do nothing. That is, they say nothing. For your patient's sake, talk! Tell her what you're going to do just before you do it. The shock value is greatly diminished that way. I usually say, "I'm going to touch the outside of your vagina and spread it apart. Now, I'm going to put my finger in. Now, relax!" That is, I used to say, "Relax!" but I don't say it anymore. What is she supposed to relax? Her hands? Her toes? Her

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[*] Department of Obstetrics and Gynecology, Thomas Jefferson University School of Medicine, Philadelphia, Pennsylvania.

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Requests for reprints should be addressed to Joni Magee, M.D., 422 West Upsal Street, Philadelphia, PA 19119.

whole body? What you specifically want her to relax is the perineal floor, the levator ani muscle. But, if you tell her that, you won't get anywhere either. So, I tell her she has a muscle she squeezes closed when she has to go and can't get to the bathroom, and she should do the opposite of that. For good measure, you push down and out from just inside the introitus and tell her to relax the muscles you are pushing on.

Now, you ask, "What are you doing with your fingers in her vagina when the speculum examination comes first?" But first a word about speculums. Many patients call them "clamps." That evokes a frightening image. A rapid explanation that you're really not going to clamp anything soothes most jangled nerves. If you really feel like talking, you can even tell her what the speculum actually does. Next, they're cold, at least the metal ones are, and the plastic ones have other drawbacks. Anyway, lubricant spoils Papanicolaou smears and gonococcal cultures, so often you can't use lubricant with a speculum. But water doesn't spoil anything. And, if by some miracle there's some hot water around, you solve two problems at once by using it on the speculum. To actually insert this device, there are two methods. Because the introitus is vertical, it seems logical to insert the speculum in the anterior posterior diameter and rotate it once it is inside. Before you do that, imagine someone's scraping a steel beam over your urethra. It's excruciating!

Back to your fingers. They allow a much kinder initial invasion than a cold, hard instrument. And while they are in the vagina, you can get a feel of the cervix so you know which way to point the speculum and how far in it needs to go. Then you put it in right over your fingers, being careful not to touch the roof of the vagina. You put it in *slowly*. Very *slowly*. Five extra seconds can prevent your patient from feeling like a rape victim. Then, you open it. This is worth a special warning, like "You'll feel like you have to go to the bathroom both ways at the same time." If you're using a plastic speculum, it locks open with a very startling click, which causes less anxiety if the patient is forewarned. It clicks again when you release it.

When you insert your fingers for the bimanual examination, slowness is again very important for comfort. Watch the patient's face. Don't ask her if it hurts; she'll tell you by her expression. You'll avoid a lot of decisions about whether a pain is significant that way. Because a pelvic examination does hurt. At least it's damned uncomfortable. And, if you asked me if it hurt when you were flipping my uterus around, I would say "Yes." Actually, it feels weird, rather than hurting. If the patient tenses up during a bimanual examination, the examiner's first reflex is to say "Relax!" But, again, this doesn't communicate specifically what you want the patient to do. "Make your belly ("abdomen," if she has a college degree) soft so I can push it and feel what's underneath it," gives the patient the feeling that she is being told what's going on and, I believe, makes her more cooperative.

The key word is "communicate." Not only does the patient have a right to know what you are doing to, and finding out about, her body, but being treated as worthy of this knowledge makes her more cooperative. I've heard of a very progressive medical school (I hope it's not apocryphal) where every male student is placed in stirrups and a strange female physician comes in, squeezes his balls, and leaves without saying a word. If you think that would make you feel hostile and insecure, you might understand why women are so ready to complain.

My suggestions should be doubly or triply adhered to if the patient is very young, or it is her first pelvic examination.

I learned my method of speculum insertion from a man and added some refinements of my own. I add this because I don't mean to imply that only a woman can, or should, be an empathetic gynecologist. But doctors only learn how patients feel by being patients or listening to them. All patients who get pelvic examinations are women, so, open your ears, men. You'll never learn from personal experience.

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Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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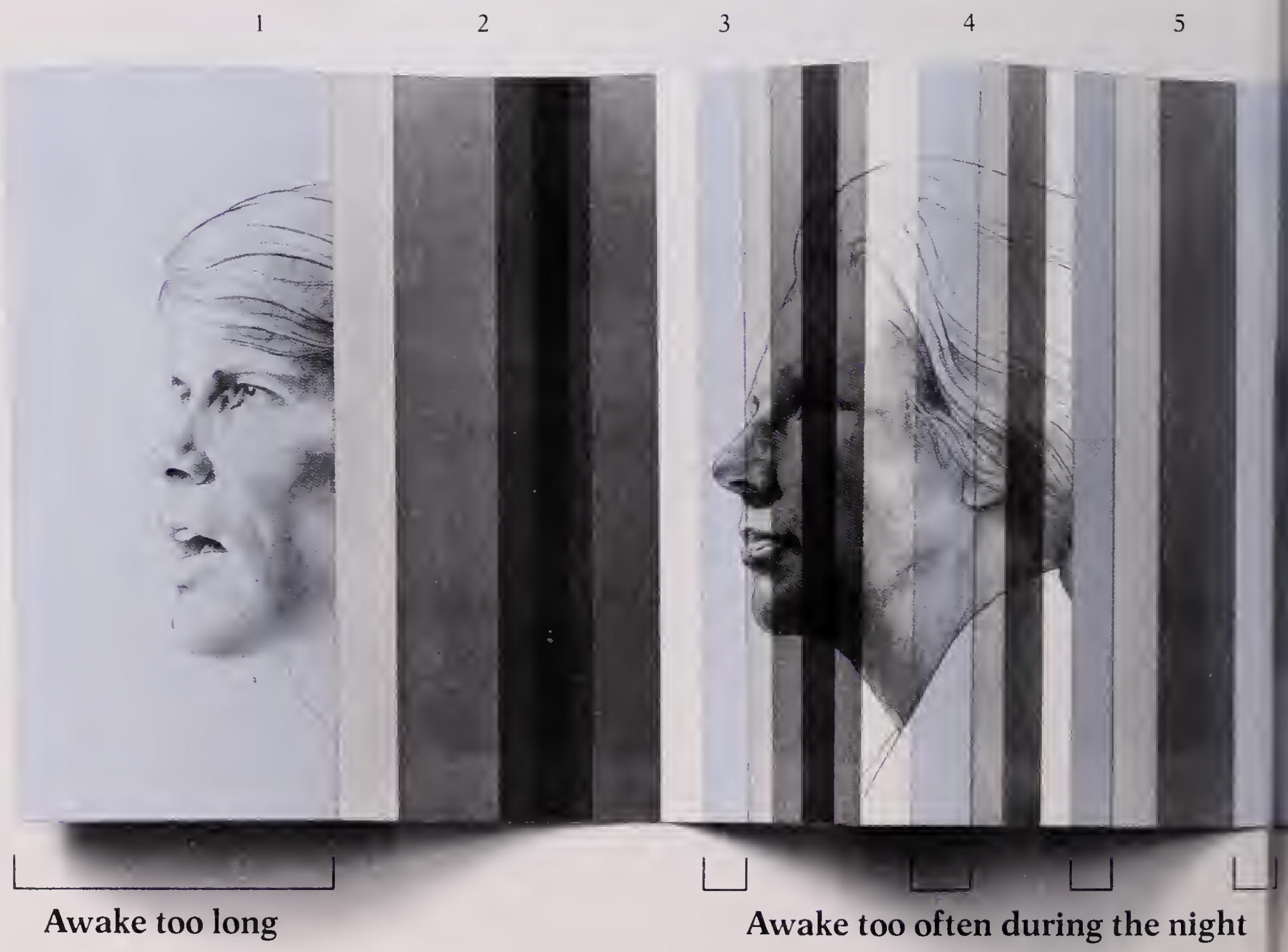
These are the most common forms of insomnia, and may occur singly or in any combination. The night of troubled sleep depicted here comprises all three types. As the night progresses from left to right, each sleep stage is identifiable by its own shade of gray. Blue represents "Awake."

As you can see, this hypothetical "patient" takes well over an hour to fall asleep, awakens several times during the middle of the night and awakens too early in the morning.

Sleep Stages

- ▭ Awake
- □ REM
- ▨ Stage 1
- ▩ Stage 2
- ■ Stage 3
- ■ Stage 4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2
3
4
5
Awake too long
Awake too often during the night

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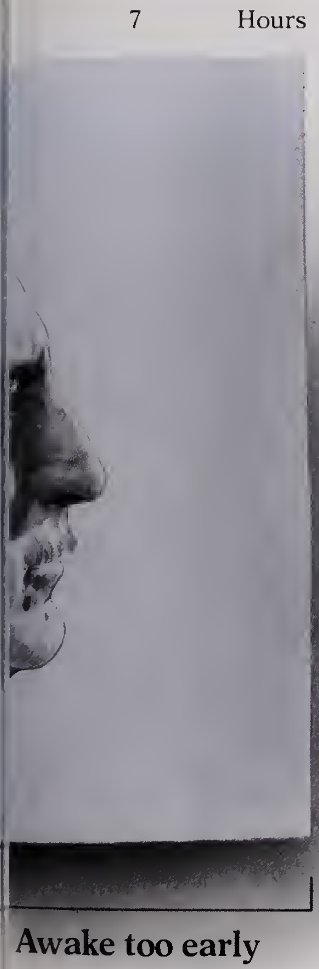
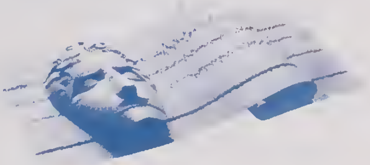


Broad-spectrum medication for the most common forms of insomnia



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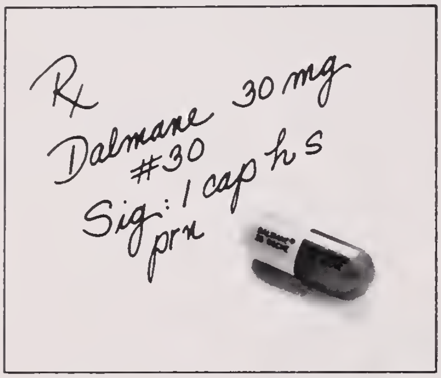

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Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum benef effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

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1. Karacan I, Williams RL, Smith JR: Th sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of th American Psychiatric Association, Washington DC, May 3-7, 1971
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3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
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Xray Conference

Large Pulmonary Nodules in a Young Man

WM. A. WILCOX, M.D.* and C. J. SWENDSEEN, M.D.*

This is the chest Xray of a 25-year-old black male who had multiple, nonspecific, complaints. He admitted to dyspnea on exertion and a recent five-pound weight loss. A low-grade fever was noted during his first few days in the hospital. Otherwise, the physical findings were normal. The hemogram and SMA-12 were within normal limits. The skin tests for Tuberculosis and triple fungus were negative. Repeated sputa were negative on the smear and culture as were bronchial washings.

The patient felt better after a few days in the hospital and was discharged to be followed as an out-patient. The chest Xray did not change during about a month of observation. The patient continued to feel fairly well.

He was readmitted for a lung biopsy. What is your diagnosis?

(See next page.)

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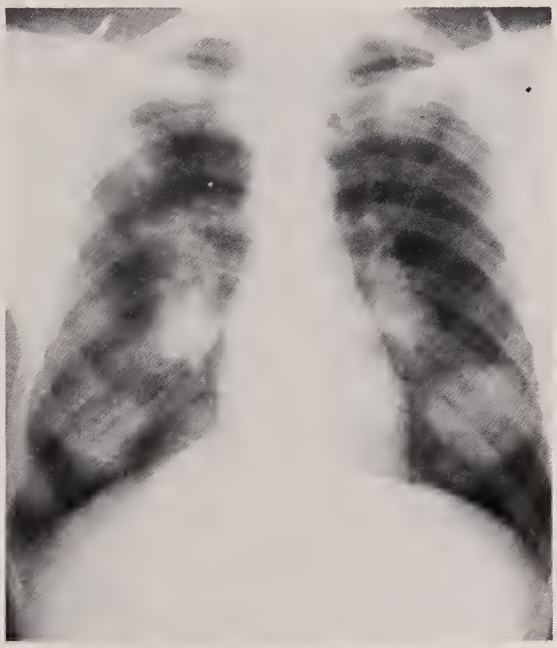
*North Memorial Medical Center, Minneapolis, Minnesota.



Figure

Diagnosis: Pulmonary Sarcoidosis

The pathological diagnosis on the pulmonary tissue was: "multiple noncaseating epithelioid granulomas consistent with pulmonary sarcoidosis."

Chest abnormalities are seen in over 90% of cases of sarcoidosis,[1] and chest Xray is the usual means of detecting the condition. Of those cases with chest involvement, lymph node enlargement is the most frequent abnormality. The type of parenchymal abnormalities which have been described are termed "reticulonodular," "fibrotic," "chronic acinar," and "large nodular."

The present case is an example of the more unusual type of parenchymal sarcoidosis. This large nodular type is seen in perhaps 2% of cases or less. Reported cases are usually blacks, often young males.[2] The appearance strongly suggests metastatic malignancy in the chest from a sarcoma or testicular primary tumor. A helpful differential point is that these sarcoid alveolar nodules will sometimes show an air bronchogram on careful inspection.[3]

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3. Reed James C and Madewell John E: The air bronchogram in interstitial disease of the lungs. Radiology 116:1, July, 1975.

Cover Painting

"Mayo Medical School Student Center"

Mr. Harold H. Crawford painted "Mayo Medical School Student Center" in early 1975. This transparent water color depicts a building long used as a center of knowledge—the Rochester Public Library and which more recently has become the focal facility of the Mayo Medical School. Mr. Crawford, architect as well as artist, originally designed this building. A graduate of the Universities of Illinois and Harvard, he has practiced architecture with Frank Chouteau Brown, Boston, 1914-1916 and as an individual architect in Rochester, Minnesota, 1916-1963. Mr. Crawford has been an artist since 1942. His works have been exhibited in various one-man and group shows. Several Crawford paintings are on permanent exhibit with the Olmsted County Historical Society.

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The National Health Planning and Resources Act: Discussion of the implications of the law, especially as it relates to planning for chirurgical and medical emergencies.

Surgical and Medical Emergencies in Obstetrics and Gynecology: Diagnosis of surgical emergencies including new diagnostic techniques; Shock in Obstetrics and Gynecology including Management of Acute Bleeding; Management of Acute Toxemia of Pregnancy.

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LOCUM TENENS WANTED—By GP in solo practice in rural community; NW Minnesota. Week of Feb. 28, 1976 to March 6. Call collect (218) 742-6231 or write W. A. Pinsonneault, M.D., Warren Clinic, Warren, Minn. 56762.

PHYSICIAN, SOUTH DAKOTA Dept. of Health. Medical Director of Maternal and Child Health and Crippled Children Program. Graduate of approved School of Medicine with pediatric and neonatal training, MPH desirable. Must be licensed to practice medicine in S.D. or eligible for license within six months. Appointment to new four year Medical faculty may be considered. Salary negotiable. Apply to: Secretary of Health, Joe Foss Bldg., Pierre, S.D. 57501.

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(Continued on page 130)

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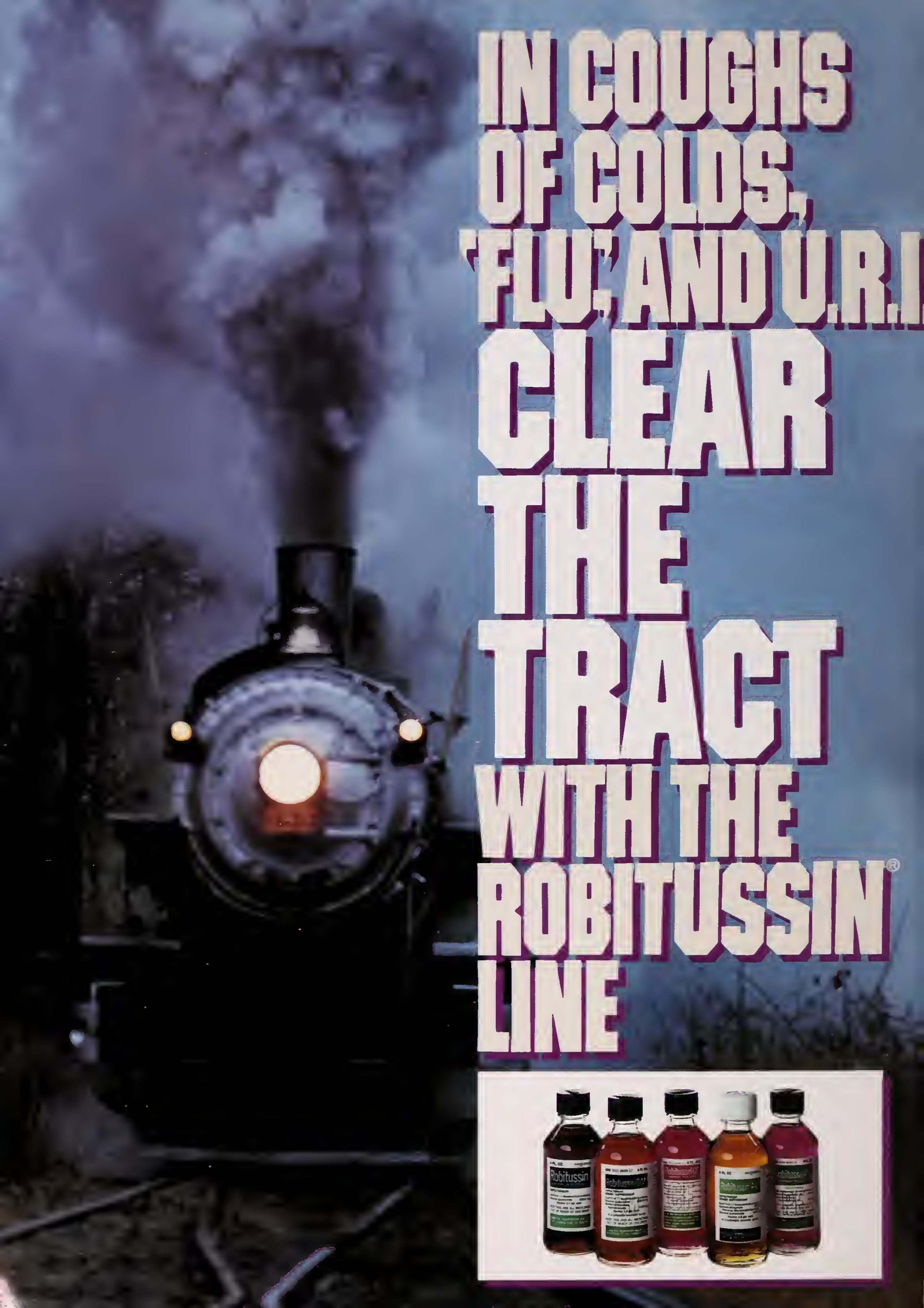
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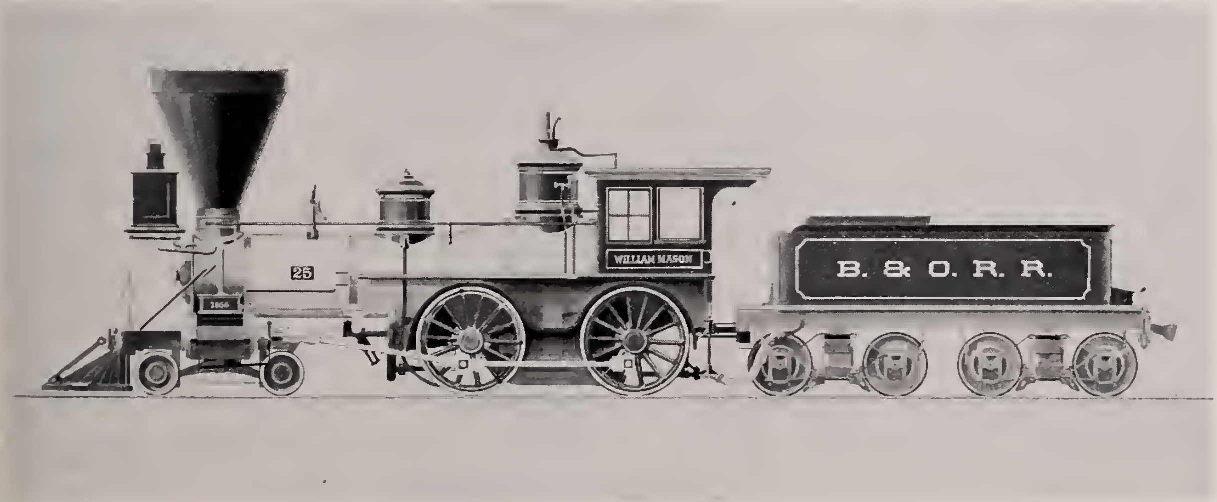

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Histoplasmosis in an Elderly Female[*]

A 67-year-old woman presented with a bilateral pulmonary infiltrate, fever and malaise.

THE PATIENT, a 67-year-old Caucasian housewife, developed her present illness on approximately August 26, 1973. Her chief complaints were weakness, malaise, nonproductive cough and fever to 101°F. She first sought the advice of her physician on August 31. Minimal auscultatory and percussion abnormalities were present on examination of the chest. A standard chest Xray indicated an interstitial pulmonary infiltrate most prominent in the right base. The interstitial markings had increased throughout both lung fields when compared to a routine chest Xray that had been taken in March 1973. She was started on Geopen which was discontinued on September 4, 1973. At that time she was subjectively improved and was beginning to experience diarrhea. A course of Vibramycin was administered orally from September 4 through September 11, 1973. Fever to 101°F. again appeared at regular intervals by mid to late September.

On October 11, 1973, she was admitted to Immanuel-St. Joseph's Hospital for complete evaluation.

Physical examination revealed a cooperative, alert, Caucasian female in no particular distress. The eye, ear, nose and throat examination was within normal limits. No breast masses were palpable. The thyroid gland was not enlarged. The heart was within normal size limits with a normal sinus rhythm. A few inspiratory rales were present in the left lung base. There was no hepatomegaly or splenomegaly. Her past medical history was noncontributory.

Laboratory Data

10-9-73. A CBC demonstrated: white blood cell count —3,500/mm^3, hemoglobin—10.5g%, hematocrit—30.9%, MCV—82 microns^3, MCH—28.8 micro-micrograms, and MCHC—34.2%. The differential count was 47% neutrophils, 23% band forms, 27% lymphocytes, 2% monocytes and 1% eosinophils. The sedimentation rate (Westergren) was 85 mm/hr. A serum protein electrophoresis demonstrated 2.7g% albumin, 0.4g% alpha$_1$globulin, 0.9g% alpha$_2$globulin, 1.1g% betaglobulin and 1.8g% gammaglobulin. The cold agglutinin titer was 1:32. A sputum specimen for cytology was nondiagnostic.

10-11-73. An SMA 12/60 profile demonstrated: calcium—8.5 mg%, inorganic phosphorus—3.4 mg%, cholesterol—190 mg%, total protein—7.0 g%, albumin—2.7 g%, total bilirubin—0.6 mg%, alkaline phosphatase—500 mU/ml, LDH—213 mU/ml, and SGOT—80 mU/ml. The anti-DNP titer was 1:1 and the anti-DNA titer was 1:1. The urinalysis was reported as follows: color—amber, character—hazy, specific gravity—1.019, pH—5.0, albumin—negative, glucose—negative, ketones—negative, occult blood—negative, red blood cells/hpf—0, casts/lpf—0, with 3+ calcium oxalate crystals.

10-13-73. A serum blastomycosis antibody complement fixation was negative. Serum histoplasmosis antibody complement fixation for mycelia was 1:16. An "M" band was present with antibody immunodiffusion for mycelia. An alkaline phosphatase fractionation was reported as 61% heat stable and was interpreted as originating from the liver.

Radiological Data

10-9-73. A chest Xray was interpreted as demonstrating acute localized pneumonitis anterior to the left hilum along with considerable enlargement in the lateral projection of the left hilum. The mass appeared to be multilobulated with poor definition of its margins.

A sternal bone marrow aspirate was performed on 10-16-73. The marrow was reported as nondiagnostic. Sputum cultures were started on 10-12-73. A scalene node biopsy was performed. Diagnostic changes were present.

Discussion

Dr. Charles Drage[†]

The history indicates an illness clinically manifest for at least seven weeks with fever and weakness as salient points. Physical examination was essentially noncontributory. Dr. Olson, would you discuss the x-ray findings?

Dr. Leroy D. Olson[‡]

Subtle changes were present in the chest Xray (Figure 1). Some of the right lung findings included linear, probably fibrotic, markings extending into the base. These followed the pattern of the bronchovascular sheath, but it was questionable that this was due to a current disease process.

There were definite changes in the left lung. The left vascular branches were obscured by a radiating infiltrate that appeared centrally, following the pattern of the bronchovascular sheaths.

The next Xrays (Figure 2) were taken in the hospital on admission. No change was demonstrated in the right lung. The right pulmonary in-

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[*] Conference held October 19, 1974 at Immanuel-St. Joseph's Hospital, Mankato.

D. K. Ohrt, M.D., Editor, and Mary E. Paul, Assistant Editor, Laboratory of Clinical Medicine, Mankato, Minnesota.

[†] Associate Professor of Medicine, Director Pulmonary Section, University of Minnesota School of Medicine.

[‡] Radiologist, Drs. Fortier and Eckert, Ltd., Mankato, Minnesota.

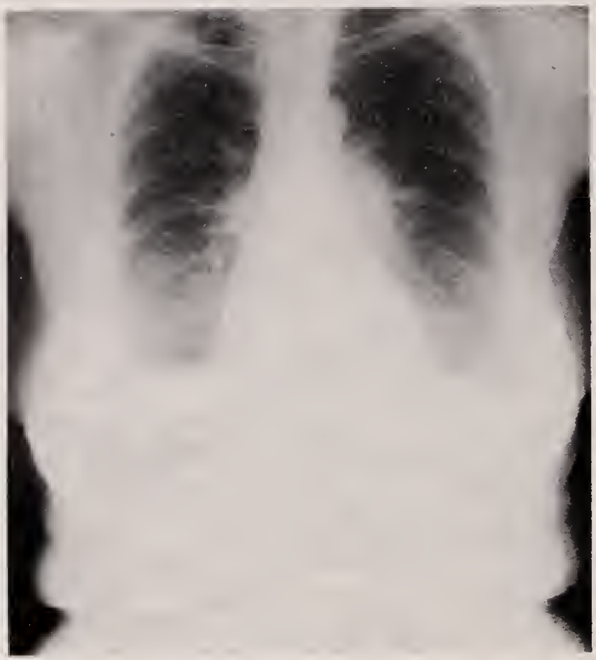

Fig. 1—September 11, 1973.

terstitial markings remained difficult to analyze. The left lung now demonstrated a relatively well demarcated zone of consolidation and an increase in the radiating pattern. The lateral film showed a region of consolidation extending anteriorly. The hilar region was obscured. Due to the radiating infiltrate, it was difficult on this radiograph to determine whether adenopathy existed.

Lateral tomograms (Figure 3) demonstrated two regions of consolidation, one of which was located in the anterior segment of the left upper lobe and another in the lingula. Both of these well demarcated consolidations extended back into the hilum. The left pulmonary artery was well defined even though superimposed on the infiltrate. There was no obvious mass compatible with adenopathy, which should demonstrate lobulations contiguous with the left pulmonary artery. Presumably some adenopathy should have been present since the infiltrate does extend posteriorly into the hilum.

The A-P tomograms demonstrated mild hilar obscuration but no definite masses.

Dr. Drage:

I will agree there was bilateral interstitial disease. The difference between pneumonic interstitial disease or fibrosis cannot be determined from Xray. There was involvement of the left hilar

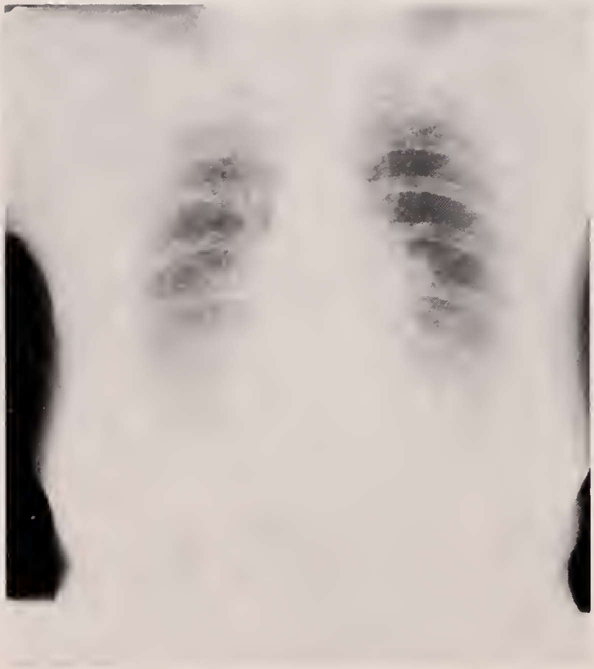

Fig. 2—October 9, 1973.

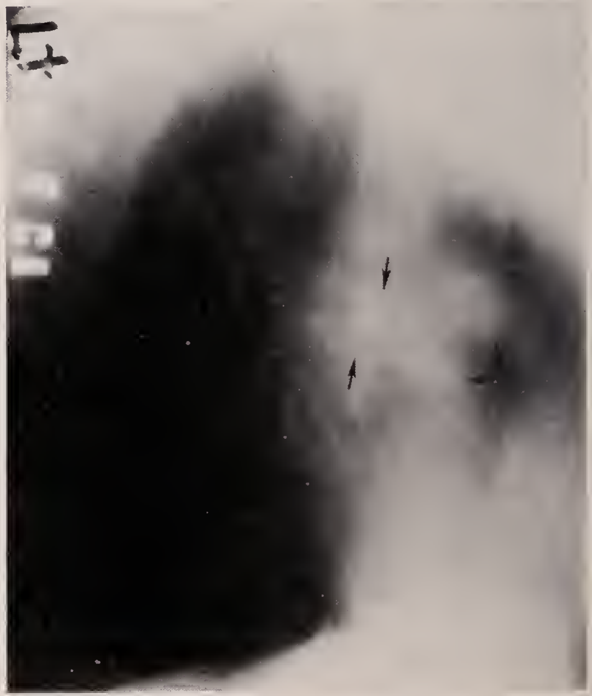

Fig. 3—October 9, 1973.

area and the anterior segment of the left upper lobe in the mass-like infiltrate but nodal involvement was questionable.

The laboratory findings strongly suggested systemic disease. The sedimentation rate was elevated The serum protein electrophoresis demonstrated hypoalbuminemia and a diffuse hypergammaglobulinemia. Decreased albumin is seen with many chronic diseases. A diffuse hypergammaglobulinemia can be seen with sarcoidosis, autoimmune disorders, lymphoproliferative diseases, chronic infection and chronic liver disease. The isolated cold agglutinin titer in this case was noncontributory. We would expect the calcium to be on the low side of normal due to the decrease in serum albumin. The cholesterol and bilirubin were normal. The alkaline phosphatase was markedly elevated and with heat fractionation was interpreted as originating in the liver. The SGOT was also mildly elevated. These values indicate significant parenchymal liver disease. The anti-DNP and DNA titers of 1:1 were non-specific. The serum histoplasmosis antibody fixation titer at 1:16 may be the most significant laboratory test. This titer can increase following a skin test. Had a skin test been performed and was a yeast phase titer obtained?

Dr. Ohrt:

The skin test was performed after the specimen for serological studies had been obtained. It was positive. The yeast phase titer was negative.

Dr. Drage:

The "M" band was present on the antibody immunodiffusion for mycelial phase of the organism. The antibody immunodiffusion for *Histoplasma capsulatum* the "M" band and the "H" band are significant. The "M" band correlates well with the complement fixation antibody obtained for the mycelial phase and if the patient has not had a skin test this is presumptive evidence of histoplasmosis. The "H" band however, is more specific since it does not appear after a skin test. A positive "M'" band and a positive "H" band on immunodiffusion is very good evidence that you are dealing with either present or past histoplasmosis. There was no "H" band reported here.[4]

Before establishing a differential diagnosis perhaps a little more detail on the patient's history might be helpful. Did she smoke, have a past exposure to tuberculosis or any exposure to birds?

Dr. Hobert J. Setzer:*

The patient had never used tobacco and had a negative tuberculin test at intermediate strength. She did not have any occupational exposure to birds although she was and is an avid gardener. I believe she made the comment that her garden was the moldiest she had ever seen. The patient had never travelled outside of the immediate upper midwest.

Dr. Drage:

Then the differential diagnosis should include sarcoidosis, fungal disease, nocardiosis, lymphoma, metastatic carcinoma and possibly bacterial infections such as psittacosis and tuberculosis. I brought up bacterial disease mainly as a differential point. I have seen one case of psittacosis which presented a chronic course similar to this case. However, with psittacosis the patient is usually very toxic and the disease runs its course in three to four weeks, sometimes lasting up to three months. This patient had already been treated with a tetracycline. So for all practical purposes psittacosis can be excluded.

This could have been tuberculosis but it is uncommon to have tuberculosis with a negative skin test. However, 15% of all active tuberculosis patients have a negative intermediate skin test according to a recent report.[12] Also, the lesion was in the anterior segment of the left upper lobe. This occurs in less than 5-10% of all cases of tuberculosis.[9] For these two reasons, (negative skin test and anterior segment involvement) I think it is relatively safe to exclude tuberculosis.

This patient was not anergic since she responded to the histoplasmin skin test. Two-thirds of all patients with documented sarcoidosis are negative to second strength PPD.[2] This patient also had obvious liver involvement. The type of sarcoidosis that presents as a febrile illness commonly occurs in patients who have accompanying liver involvement. The interstitial infiltrate this patient developed could be due to sarcoidosis. Unilateral hilar involvement would be evidence against sarcoidosis but would not completely exclude it. Sarcoidosis fits into the differential diagnosis but with the information I was given I am eliminating it.

We cannot exclude tumor with this clinical presentation. Also, we may be dealing with more than one disease. It is not uncommon to see lung tumor and tuberculosis together. Occasionally, we have seen histoplasmosis or cryptococcosis with tumors. With bilateral interstitial disease you could postulate that this was a lymphangitic spread of a primary tumor of the lung or an unusual manifestation of alveolar cell carcinoma but these would be unlikely explanations.

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*Internist, Mankato Clinic, Mankato, Minnesota.

Metastatic disease cannot be excluded. A carcinoma of the breast can produce an interstitial pattern with concomitant hilar node involvement or a localized pneumonic process. Metastatic tumor from the breast with lymphangitic spread is a possibility.

I will discuss the leukemias and lymphomas together. I would expect that the bone marrow would have been diagnostic in a leukemic process causing a pneumonic infiltrate and hilar enlargement. Lymphoma of the lung can be present with interstitial and lymphatic involvement, pulmonary consolidation and hilar adenopathy. I would expect evidence of bone marrow invasion if the liver was involved to this extent.

My first choice for a diagnosis would have to be disseminated histoplasmosis with involvement of the liver and the lungs.[8] The patient had an interstitial pulmonary disease, fever and chills. The serological studies, while not diagnostic, would be very suggestive of histoplasmosis. It is important to establish this diagnosis since the disease can be successfully treated with amphotericin-B.[15,17,19] My second choice would be a malignancy, either a primary lung tumor or metastatic disease with lymphangitic involvement. If this case represents histoplasmosis, it was probably relatively acute because the patient showed no evidence of cavitation which is present in the more chronic type of histoplasmosis, primarily in the upper lobes.[11,16] The histoplasmosis was probably not localized in the lungs because of evidence of liver involvement.

Let us go over what could have been done to make the diagnosis. We know we are dealing with a systemic disease. We could look at other organ systems. Other useful studies might have been (in order of complication), bone marrow, liver biopsy, mediastinoscopy and bronchoscopy with transbronchial biopsy. I would have done a bone marrow first because there is a good chance that you are dealing with a fungal infection or tumor. You might have found tumor in the bone marrow or been able to identify the noncaseating granulomas of sarcoidosis or a fungus.

Dr. Ohrt:

A bone marrow aspirate was performed early in the course of her clinical work-up for evaluation of leukopenia. There were numerous myeloid precursors. The study offered no other diagnosis at the time. After the scalene node biopsy we looked at the marrow again and found the diagnosis was apparent.

Dr. Drage:

I would have considered a liver biopsy next because it is a relatively simple procedure. There may have been evidence of histoplasmosis, sarcoidosis or tumor in the liver.

Dr. Ohrt:

I do not think a liver biopsy was necessary because the diagnosis had already been made.

Dr. Drage:

If the diagnosis could not have been made from the bone marrow or the liver biopsy I would follow with either mediastinoscopy or scalene node biopsy. Scalene node biopsy is not always as definitive a test as mediastinoscopy in lung disease. The scalene nodes often contain the noncaseating granulomas associated with sarcoidosis. However, in one study up to 5% of the cases had

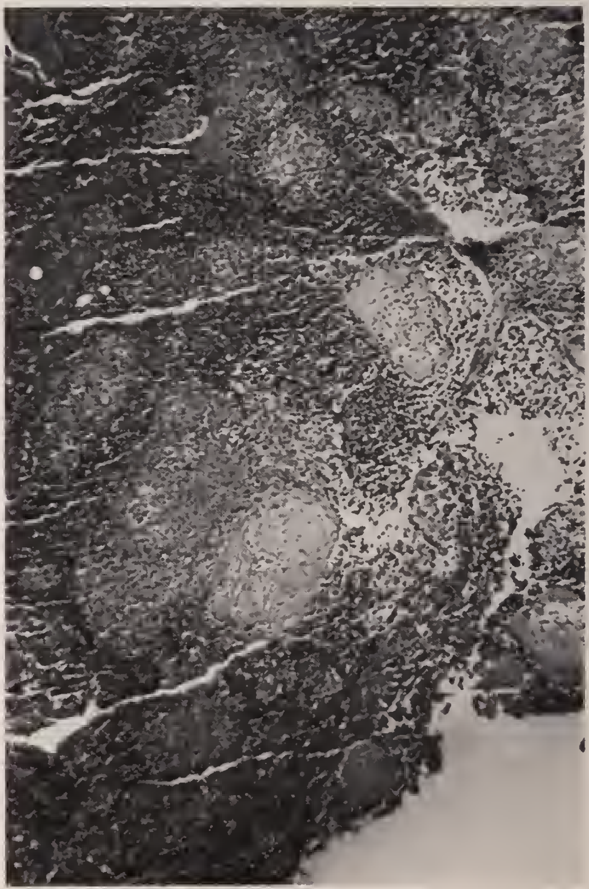

Fig. 4—Scalene node with numerous noncaseating granulomas, 100X.

misleading changes in the scalene nodes. The correct diagnosis was obtained with mediastinoscopy.[7]

If mediastinoscopy did not produce a diagnosis I would have recommended bronchoscopy and transbronchial biopsy. In this case you may have been able to obtain yeast with brushings. Our tissue diagnosis success is approximately 85% with transbronchial biopsy.[18]

Dr. Ohrt:

Sections of the scalene nodes demonstrated nests of epithelioid cells similar to those one would see in sarcoidosis (Figure 4). These areas were rimmed by mature lymphocytes. The nodes had not been involved very long. Epithelioid cells take approximately a week to develop to produce a lesion such as this.[3] Typical giant cells were rarely seen. It takes roughly two to three weeks for the giant cells to develop. Caseation necrosis was not identified in the biopsy specimen. Typical small budding yeasts were observed in the scalene nodes (Figure 5) with Gomori's methenamine silver stain. In our experience the PAS stain is a poor method for demonstration of *H. capsulatum.* A bone marrow aspirate was cultured with growth of a dimorphic fungus which eventually produced the typical tuberculate chlamydospores of *H. capsulatum.* The sputum also produced a positive culture.

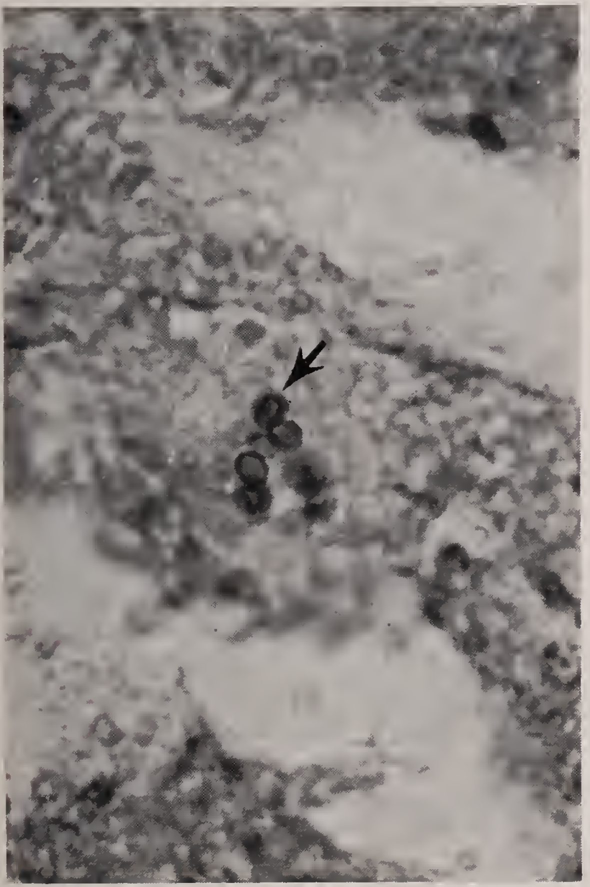

Fig. 5—Multiple small yeasts characteristic of *Histoplasma capsulatum* (Gomori's methenamine silver technique), 1000X.

Ten days after the skin test had been applied the complement fixation titer for mycelia was 1:32 and antibody complement fixation for yeast 1:512. A titer of 1:512 is virtually diagnostic in this particular instance even if the skin test had been applied. The skin test will increase the mycelial phase more than a factor of two.[13]

The source of infection in this lady is not known. *H. capsulatum* was not grown from the soil in her garden. She had no known exposure to bird or bat excreta. Acute disseminated histoplasmosis usually follows heavy exposure.[6,14] The initial soft pulmonary infiltrates gradually harden over the next few weeks. Hilar adenopathy usually accompanies the initial phase and may subside somewhat during the next several weeks. This lady may have a significant alteration of cellular immunity. Interplay between susceptibility of the reticuloendothelial system to infection and vigor of host tissue reactions determine the outcome of the initial invasion. Without vigorous treatment the mortality approaches 100% once dissemination has occurred.[15] Dr. Setzer, would you please comment on the treatment of this particular patient?

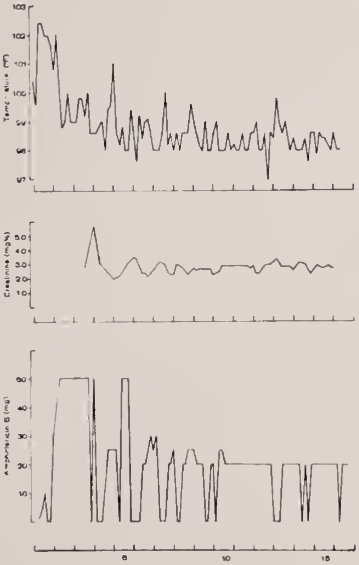

Fig. 6—Comparison of temperature response and creatinine levels with amphotericin-B therapy.

Dr. Setzer:

At the time we were notified there was a definite growth being obtained in the laboratory. Amphotericin-B therapy was initiated with very small trial doses. Then we increased the dosage to a 50 mg. infusion over a six-to-eight-hour period. She tolerated the high dose of amphotericin-B for the first three weeks. There was then a rapid rise in the creatinine and the drug was withheld.[5] In the initial course her fever reached 102°F and with the amphotericin-B the fever responded quite dramatically (Figure 6). Her liver function studies did not change markedly over this period.

Due to the rapid rise in creatinine, the total dose was reduced to 20 mg. daily. We had periods when therapy had to be stopped for as long as five to six days when the creatinine reached high levels. Clinically, she had few side effects outside of a period of nausea early in the course. She received a total of 2.2 g over a period of approximately three months. It is necessary that these patients be administered between 2-2.5 g of amphotericin-B. If the dosage is below that level there is a fairly high incidence of recurrence.[1]

The adrenal glands are often involved and an acute Addisonian crisis can occur during the course of the disease. Two serum cortisol levels during her course were reported as normal.

Dr. Drage:

I am certainly glad you were as aggressive as you were in making more sections and using fungal stains. The initial histopathology looked like noncaseating granulomas of sarcoidosis. The diagnosis must be pursued aggressively in a case like this because treatment for sarcoidosis with steroid therapy can be extremely harmful in a case of unrecognized histoplasmosis.

Dr. Ohrt:

Dr. Drage, how reliable are serological tests in cases like this and what is your plan for follow-up?

Dr. Drage:

Serological testing is not always reliable. Values are hard to interpret in patients who have had a prior skin test.[10] The results also may vary as much as four-fold from laboratory to laboratory. However, when the clinical presentation looks like this they are extremely helpful.

After adequate amphotericin-B therapy I follow the patients on a six weeks basis with fungal serologies. If the serologies are gradually falling, the pulmonary lesion clearing and *H. capsulatum* is not obtained from the sputum in a patient who is relatively assymptomatic, you can be satisfied with the therapy. I would expect that this patient's yeast serologies would decrease to 1:32, to 1:16 and even lower. They will stay elevated for a number of years. The patient should be followed initially at six week intervals for six months, then three month intervals, then six month intervals and then on a yearly basis. The patient must know that if symptoms appear he should notify his physician.

Dr. Drage's diagnosis: Disseminated histoplasmosis, R.O. metastatic carcinoma with possible lymphangitic spread.

Final diagnosis: Acute disseminated histoplasmosis.

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CHOLESTEROL

CONSIDER

Choloxin®

Sodium Dextrothyroxine)

Proven Cholesterol-Lowering Adjunct to Diet.

effective agent for low density lipoproteins in
thyroid, Non-Cardiac Patients.

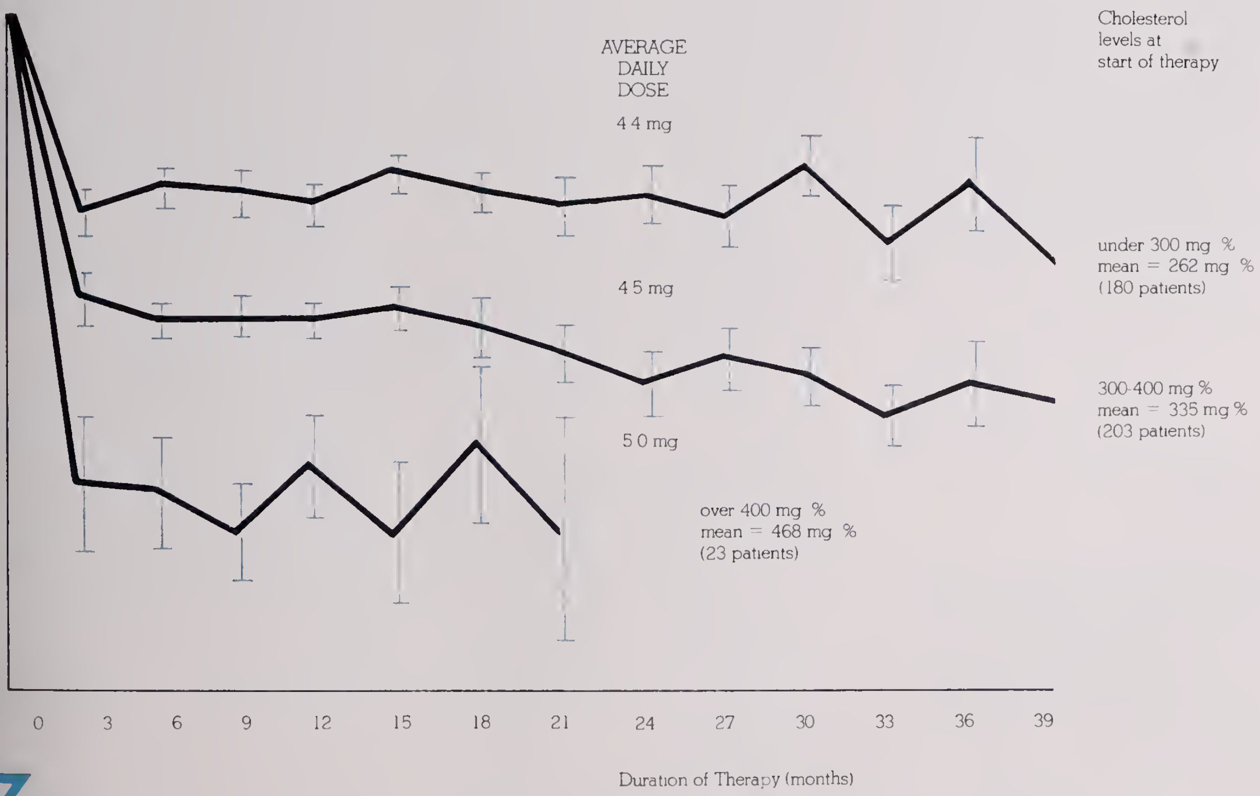
IOLOXIN® (Sodium Dextrothyroxine) is the con-
ient and practical way to manage the hard-to-
nage patient who doesn't always follow the diet
gimen that you've outlined.

nvenient once-a-day dosage encourages patient
operation, and it's economical for long-term
rapy.

AN IMPORTANT NOTE:
It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question.

CHOLOXIN (Sodium Dextrothyroxine) is a thyroid analogue which effectively lowers elevated serum cholesterol 15 to 35% (see chart below) in low density lipoproteins.

CHOLOXIN (Sodium Dextrothyroxine) has undergone ten years of clinical trials and seven years of practice. The clinical trials consisted of 337 clinical studies involving over 3,000 hypercholesterolemic non-cardiac patients. It is among the most thoroughly evaluated drugs ever presented to physicians.



NOT ALL PATIENTS ARE REPRESENTED AT EACH TIME INTERVAL

LINT LABORATORIES
ISION OF TRAVENOL LABORATORIES, INC.
erfield, Illinois 60015

NOTE:
See following page for full prescribing information.

Choloxin
(Sodium Dextrothyroxine)

Effectively Lowers Elevated Cholesterol With Convenient Once-A-Day Dosage

Four strengths 1, 2, 4, and 6 mg are available making the scored tablet regimen a flexible dosage system And, for most patients, CHOLOXIN tablets offer once-a-day dosage

CHOLOXIN* (sodium dextrothyroxine) Single-Tablet-A-Day Dosage Schedules

See prescribing information in package insert reproduced below

	Starting Dosage	Increased Monthly by	Usual Maintenance	Maximal Recommend
Adult Hypercholesterolemic	1 0-2 0 mg	1 0-2 0 mg	4 0-8 0 mg	4 0-8 0 mg
Pediatric Hypercholesterolemic	0 05 mg /kg body weight	0 05 mg /kg	0 1 mg /kg body weight	4 0 mg
Hypothyroid Cardiac	0 5 1 0 mg	1 0 mg	4 0 mg	4 0 mg

Description
CHOLOXIN (sodium dextrothyroxine) is the sodium salt of the dextrorotatory isomer of thyroxine It is chemically described as D-3 5 3 5 tetraiodothyronine sodium salt

Actions
The predominant effect of CHOLOXIN (sodium dextrothyroxine) is the reduction of serum cholesterol levels in hyperlipidemic patients Beta lipoprotein and triglyceride fractions may also be reduced from previously elevated levels

Most of the available evidence indicates that CHOLOXIN stimulates the liver to increase catabolism and excretion of cholesterol and its degradation products via the biliary route into the feces Cholesterol synthesis is not inhibited and abnormal metabolic end-products do not accumulate in the blood

Indications
This is not an innocuous drug Strict attention should be paid to the indications and contraindications.

CHOLOXIN (sodium dextrothyroxine) is an antilipidemic agent used as an adjunct to diet and other measures for the reduction of elevated serum cholesterol (low density lipoproteins) in euthyroid patients with no known evidence of organic heart disease

The drug is also indicated in the treatment of hypothyroidism in patients with cardiac disease who cannot tolerate other types of thyroid medication **Before prescribing, note the following Results from a randomized clinical study have indicated a possible adverse effect when CHOLOXIN (sodium dextrothyroxine) is administered to a patient receiving a digitalis preparation There may be an additive effect This additive effect may possibly stimulate the myocardium excessively in patients with significant myocardial impairment. CHOLOXIN (sodium dextrothyroxine) dosage should not exceed 4 mg per day when the patient is receiving a digitalis preparation concomitantly Careful monitoring of the total effect of both drugs is important.**

It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease Several years will be required before current investigations will yield an answer to this question

Contraindications
The administration of CHOLOXIN (sodium dextrothyroxine) to euthyroid patients with one or more of the following conditions is contraindicated

1 Known organic heart disease including angina pectoris history of myocardial infarction cardiac arrhythmia or tachycardia either active or in patients with demonstrated propensity for arrhythmias rheumatic heart disease history of congestive heart failure and decompensated or borderline compensated cardiac status
2 Hypertensive states other than mild labile systolic hypertension
3 Advanced liver or kidney disease
4 Pregnancy
5 Nursing mothers
6 History of iodism

Warnings
CHOLOXIN (sodium dextrothyroxine) may potentiate the effects of anticoagulants on prothrombin time Reductions of anticoagulant dosage by as much as 30% have been required in some patients Consequently, the dosage of anticoagulants should be reduced by one-third upon initiation of CHOLOXIN (sodium dextrothyroxine) therapy and the dosage subsequently readjusted on the basis of prothrombin time The prothrombin time of patients receiving anticoagulant therapy concomitantly with CHOLOXIN (sodium dextrothyroxine) therapy should be observed as frequently as necessary, but at least weekly, during the first few weeks of treatment.

In the surgical patient it is wise to consider withdrawal of the drug two weeks prior to surgery if the use of anticoagulants during surgery is contemplated

When CHOLOXIN (sodium dextrothyroxine) is used as thyroid replacement therapy in hypothyroid patients with concomitant coronary artery disease especially those with a history of angina pectoris or myocardial infarction or other cardiac disease treatment should be initiated with care Special consideration of the dosage schedule of CHOLOXIN (sodium dextrothyroxine) is required This drug may increase the oxygen requirements of the myocardium especially at high dosage levels Treated subjects with coronary artery disease must be seen at frequent intervals If aggravation of angina or increased myocardial ischemia cardiac failure or clinically significant arrhythmia develops during the treatment of hypothyroid patients the dosage should be reduced or the drug discontinued

Special consideration must be given to the dosage of other thyroid medications used concomitantly with CHOLOXIN (sodium dextrothyroxine As with all thyroactive drugs hypothyroid patients are more sensitive to a given dose of CHOLOXIN (sodium dextrothyroxine) than euthyroid patients

Epinephrine injection in patients with coronary artery disease may precipitate an episode of coronary insufficiency This condition may be enhanced in patients receiving thyroid analogues These phenomena should be kept in mind when catecholamine injections are required in sodium dextrothyroxine-treated patients with coronary artery disease

Since the possibility of precipitating cardiac arrhythmias during surgery may be greater in patients treated with thyroid hormones it may be wise to discontinue CHOLOXIN (sodium dextrothyroxine) in euthyroid patients at least two weeks prior to an elective operation During emergency surgery in euthyroid patients and in surgery in hypothyroid patients in whom it may not be advisable or possible to withdraw therapy the patients should be carefully observed

There are reports that sodium dextrothyroxine in diabetic patients is capable of increasing blood sugar levels with a resultant increase in requirements of insulin or oral hypoglycemic agents Special attention should be paid to parameters necessary for good control of the diabetic state in dextrothyroxine-treated subjects and to dosage requirements of insulin or other antidiabetic drugs If sodium dextrothyroxine is later withdrawn from patients who required an increase of insulin (or oral hypoglycemic agents) dosage during its administration the dosage of antidiabetic drugs should be reduced and adjusted to maintain good control of the diabetic state

When either or both impaired liver or kidney function are present the advantages of CHOLOXIN (sodium dextrothyroxine) therapy must be weighed against the possibility of deleterious results

Usage in Women of Childbearing Age
Women of childbearing age with familial hypercholesterolemia or hyperlipemia should not be deprived of the use of this drug it can be given to those patients exercising strict birth control procedures Since pregnancy may occur despite the use of birth control procedures administration of CHOLOXIN (sodium dextrothyroxine to women of this age group should be undertaken only after weighing the possible risk to the fetus against the possible benefits to the mother Teratogenic studies in two animal species have resulted in no abnormalities in the offspring

Precautions
It is expected that patients on dextrothyroxine therapy will show greatly increased serum protein bound iodine levels These increased serum PBI values are evidence of absorption and transport of the drug and should NOT be interpreted as evidence of hypermetabolism similarly they may not be used for titrating the effective dose of CHOLOXIN sodium dextrothyroxine PBI values in the range of 10 to 25 mcg% in treated patients are common

If signs or symptoms of iodism develop during CHOLOXIN sodium dextrothyroxine therapy the drug should be discontinued

A few children with familial hypercholesterolemia have been treated with CHOLOXIN sodium dextrothyroxine for periods of one year or longer with no adverse effects on growth However it is recommended that the drug be continued in patients in this age group only if a significant serum cholesterol lowering effect is observed

Adverse Reactions
The side effects attributed to dextrothyroxine therapy are for the most part due to increased metabolism and may be minimized by following the recommended dosage schedule Adverse effects are least commonly seen in euthyroid patients with no signs or symptoms of organic heart disease the incidence of adverse effects is increased in hypothyroid patients and is highest in those patients with organic heart disease superimposed on the hypothyroid state

In the absence of known organic heart disease some cardiac changes may be precipitated during sodium dextrothyroxine therapy In addition to angina pectoris arrhythmia consisting of extrasystoles ectopic beats or supraventricular tachycardia ECG evidence of ischemic myocardial changes and increase in heart size have been observed Myocardial infarctions both fatal and non fatal have occurred but these are not unexpected in untreated patients in the age groups studied It is not known whether any of these infarcts were drug related

Changes in clinical status that may be related to the metabolic action of the drug include the development of insomnia nervousness palpitations tremors loss of weight lid lag sweating flushing hyperthermia hair loss diuresis and menstrual irregularities Gastrointestinal complaints during therapy have included dyspepsia nausea and vomiting constipation diarrhea and decrease in appetite

Other side effects reported to be associated with CHOLOXIN (sodium dextrothyroxine) therapy include the development of headache changes in libido (increase or decrease) hoarseness tinnitus dizziness peripheral edema malaise tiredness visual disturbances psychic changes paresthesia muscle pain and various bizarre subjective complaints Skin rashes including a few which appeared to be due to iodism and itching have been attributed to dextrothyroxine by some investigators Gallstones have been discovered in occasional dextrothyroxine-treated patients and cholestatic jaundice has occurred in one patient although its relationship to CHOLOXIN (sodium dextrothyroxine) therapy was not established

In several instances the previously existing conditions of the patient appeared to continue or progress during the administration of CHOLOXIN (sodium dextrothyroxine) a worsening of peripheral vascular disease sensorium exophthalmos and retinopathy have been reported

CHOLOXIN (sodium dextrothyroxine) potentiates the effects of anticoagulants such as warfarin or Dicumarol on prothrombin time thus indicating a decrease in the dosage requirements of the anticoagulants On the other hand dosage requirements of antidiabetic drugs have been reported to be increased during dextrothyroxine therapy (see WARNINGS section)

Dosage and Administration
For **adult** euthyroid hypercholesterolemic patients the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is 4 to 8 mg per day The initial daily dose should be 1 to 2 mg to be increased in 1 to 2 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily if that dosage level is indicated to effect the desired lowering of serum cholesterol

When used as partial or complete substitution therapy for levothyroxine in hypothyroid patients with cardiac disease who cannot tolerate other types of thyroid medication the initial daily dose should be 1 mg to be increased in 1 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily preferably the lower dosage The maximum in patients receiving digitalis therapy is 4 mg

For **pediatric** hypercholesterolemic patients the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is approximately 0 1 mg (100 mcg) per kilogram The initial daily dosage should be approximately 0 05 mg (50 mcg) per kilogram to be increased in up to 0 05 mg (50 mcg) per kilogram increments at monthly intervals The recommended maximal dose is 4 mg daily if that dosage is indicated to effect the desired lowering of serum cholesterol

If new signs or symptoms of cardiac disease develop during the treatment period the drug should be withdrawn

How Supplied
CHOLOXIN (sodium dextrothyroxine) is supplied in prescription packages of scored 1 2 4 and 6 mg tablets

March 1975

FLINT LABORATORIES
DIVISION OF TRAVENOL LABORATORIES, INC
Deerfield, Illinois 60015

Special Article

Implementation of an Expanded Emergency System

St. Paul, Minnesota Experience

BRIAN C. CAMPION, M.D.,* JOHN W. McBRIDE, M.D.,* PRADUB SUKHUM, M.D.*
and ROBERT A. van TYN†

Expanded emergency systems to include mobile coronary care have been increasingly used in the United States in recent years. St. Paul, Minnesota implemented such a system in August, 1973. This community wide system is operated by the Fire Department in conjunction with St. Paul-Ramsey Hospital, the city-county hospital. Such a system is described with reasons given for certain methods which have been used. Alternative methods are described where applicable.

THAT A LARGE PERCENTAGE of deaths from acute myocardial infarction occur outside of the hospital prior to availability of any type of definitive medical care is well known. Pantridge, by implementing his "flying squad" was the first in the western world to develop the concept of moving coronary care to the patient's bedside.[1] His unit, staffed by physicians and nurses, is prepared to remain with the patient using coronary care unit procedures until stabilization has occurred, and only then is transportation to the hospital undertaken.

Several areas in this country have been pioneers in mobile coronary care, with some significant differences.[2-6] Instead of a single dedicated unit, several fully equipped ambulances have been located strategically throughout the community, which considerably decreases response time. In addition, rather than staffing the units with physicians and nurses, trained paramedical personnel have been utilized with hospital communication and ECG monitoring at the base hospital, where physicians direct care based on data obtained by the paramedics. Several centers, including Jacksonville, Seattle, and Los Angeles, have demonstrated that it is possible to train paramedical personnel to function effectively.[4-6] Nagel has pointed out that trauma, drowning, electrocution, and other medical crises may utilize the facilities of mobile coronary care to deliver a more effective quality of emergency care.[5]

The concept of an expanded emergency system, including mobile coronary care, is not universally accepted, although many communities have moved in this direction in restructuring emergency services. The federal government has published guidelines for training expanded emergency medical technicians and monies for equipment have been made available through the Department of Transportation. St. Paul, Minnesota implemented such a system in August of 1973. We believe that it is of value to others to describe the considerations and problems involved in bringing this system to reality in our community.

Providers of an Expanded Emergency System

Our system consists of physicians at St. Paul-Ramsey Hospital, the city-county hospital, working closely with the St. Paul Fire Department to provide this service to the citizens of St. Paul, Minnesota. The hospital base station, where care is directed, must have a physician available twenty-four hours per day, seven days per week. This is possible in teaching hospitals, hospitals with twenty-four hour per day emergency service, or where appropriate portable communication equipment is selected, allowing physicians to be reached at any time and at any place.

While not commonly practiced, the coronary

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See editorial, page 93.

care aspects of this system might be supervised by a coronary care unit nurse, either riding on the ambulance operating under standing orders, or by voice communication from a coronary care unit. The legality and desirability of this last alternative is not settled. One concern is that emergency room physicians do not have adequate experience with coronary care to handle the multivariant problems. When possible, communications with physicians skilled in cardiology is advisable. We feel a teaching hospital with internal medicine residents who are available twenty-four hours a day is the best of the above alternatives for the coronary care segment. Other emergencies are best handled by an emergency room physician who is familiar with these medical conditions. We therefore decided to use both the coronary care unit personnel with their expertise and the emergency room physicians to provide the best service through dual communication systems which are available but more expensive.

Provider of Service

The provider of the service may be public or private. Fire departments, law enforcement agencies and private ambulance companies have been used. In most medium to large communities "short response times" are impossible unless multiple vehicles stationed throughout the community are used. Departure from a single centrally located point gives unacceptably long response times to outlying areas. Public services, such as fire and police, function by covering districts and are so located as to minimize response time.

Education Process

The education process is quite long and requires in most projects, a fulltime commitment by the student. Large pools of men are needed to cover existing services during the training period. This is problematic for any provider, but since the Fire Chief of St. Paul was willing to provide the men on this basis, the Fire Department seemed the most viable alternative. Other community situations are clearly different and no blanket statement as to the best provider is applicable.

A vital ingredient in implementing this system is close work and cooperation between the physician directors and the service providers. Mutual respect for problems unique to each area is essential. In our experience, this factor of cooperation is more important than the type of equipment, provider, or any other single element.

Candidate Selection

All of our initial thirty-three men have had, as a minimum, advanced first aid training. Many of them had previously ridden Fire Department ambulances and all were volunteers. While initially we tended to avoid older men, we no longer do so because their performance has been good both during the educational segment and later in service.

Education

The paramedics must serve as the eyes and ears of the physician in the field; therefore, no program is stronger than his ability to evaluate a patient. We know of no better way to obtain these skills than extensive patient contact by the paramedic student; so, a hospital setting was chosen.

Duration and depth of the curriculum depends on the degree of independent function the paramedic will have in actual practice. Since the potential for breakdown in the communication system is ever present, we felt that the men must be trained to function independently. In our system this required a 640 hour training course.

Anatomy, Physiology, Medical Terminology and Basic Skills

This two week, eighty hour segment was oriented toward the delivery of emergency care. Autopsies were used to demonstrate anatomic relations. Basic introduction to obtaining data utilized an organ system orientation. A course in medical terminology was also given because of its obvious importance in communications. The Anatomy, Physiology and Medical Terminology course required a great deal of outside study and was the most difficult part of the course for men who oftentimes had been away from didactic education for many years. An introduction to skills such as venipuncture, drawing up medications, obtaining vital signs and starting IV's was also provided during this phase. Evaluation of this segment was done by daily testing.

Coronary Care Segment

The Coronary Care segment was subdivided into a didactic portion of four weeks duration (160 hours) and a clinical portion of two weeks (80 hours). The men took a course similar to that offered to the hospital's registered nurses in coronary care. The nursing skills portion was excluded with increased emphasis on monitoring techniques, history and physical examination.

We used the ROCOM multimedia instruction system with a fulltime coronary care unit, nurse-educator supplementing the material. We feel a fulltime instructor is mandatory since the ROCOM system, while quite good, provides only basic information and is severely lacking in some areas. In addition, many physician lectures, plus small work group sessions were included. Arrhythmias and cardiovascular pharmacology were strongly emphasized. A two week practical period was spent in several coronary care units in St. Paul, always with a fulltime nurse instructor and supplemental physician rounds in small group sessions. Intensive practice in history and physical examination of the cardiovascular system was included utilizing actual patients and including situational problem-solving.

Evaluation was by pre-, intermediate, and post-testing.

Emergency Medical Technician Segment

This segment was divided into several areas:

1. A basic thirty hour didactic lecture course consisted of one hour per day of lectures designed to cover all non-cardiac emergencies.

2. Daily rounds with the blood drawing team supplemented practical skills. Hospital personnel cooperated by allowing the student paramedics to perform applicable procedures wherever possible.

3. Small groups of three to four men rotated in the following areas:

a. Emergency room where patient evaluation, observation and participation in emergency procedures were stressed. During this time some exposure to pediatric emergencies was provided.

b. Operating room where the men learned to place the esophageal airway under the supervision of anesthesiologists and nurse anesthetists, start IV's and observe surgery. During surgical observation, anatomy, control of bleeding, and definitive procedures for emergencies was stressed. We also felt it important that the men realize what happened to the emergency patients once they arrived in the hospital. Observation of deliveries with emphasis on emergency care was included in this segment.

c. Small group sessions in pulmonary disease, neurology, gastroenterology, endocrinology and psychiatry utilized physician tutors reviewing histories and physical examinations and providing practical information on the evaluation and care of emergencies seen in these specialized areas.

d. Time was spent in the medical and surgical intensive care units and the burn unit learning evaluation and practical care including moving and transportation of sick and injured patients.

This total segment required six weeks (240 hours). Students were evaluated by a written and practical test at the end of this segment.

Internship

This two week segment was designed to familiarize the men with the operations of the paramedic units as well as procedures and equipment. After two units were in service we began an internship where student paramedics rode as extra men on units already in service. During this segment, practical application of new and learned skills under the tutelage of more experienced paramedics was possible. Furthermore, standard operating procedures and communication skills were learned. The internship helped us to activate two additional units with less difficulty.

We are currently evaluating the education system. While changes will be made, the basic format will remain the same. We must stress the importance of patient evaluation, history and physical examination, and accurate data recording, since the system will be only as strong as the paramedic is well trained.

Continuing Education

After the initial educational program a strong continuing education program must serve to review principles previously learned, evaluate job performance, and add new materials. Each man receives six to ten hours of ongoing education per month, divided into three segments:

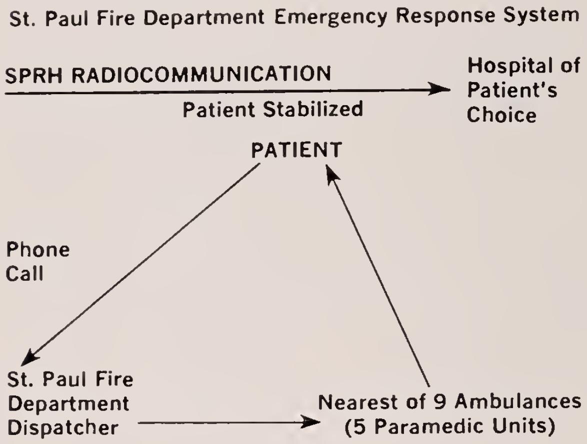
1. A two-hour-monthly session includes all the paramedics. This allows us to easily add new material and to share information among units.

2. One hour sessions in the fire stations in smaller groups where individual run reports may be reviewed critically.

3. In-hospital training where small groups continue practice in patient evaluation and previously learned information may be reemphasized.

Operation: (Figure)

While ideally the "911" number for all emergencies is preferable, this system is not yet available to us. The St. Paul Fire Department may be dialed by any citizen experiencing an emergency. The dispatcher attempts to get maximum information in a short period of time, but has neither the training nor background to make medical decisions. We have not felt further training advantageous because the reliability of information obtained under an emergency situation by telephone is questionable.


St. Paul Fire Department Emergency Response System
SPRH RADIOCOMMUNICATION
Patient Stabilized
Hospital of Patient's Choice
PATIENT
Phone Call
St. Paul Fire Department Dispatcher
Nearest of 9 Ambulances (5 Paramedic Units)

Figure

There are currently nine St. Paul Fire Department ambulances, five of which are paramedic units. Each of these nine units covers a district the outskirts of which is no more than four to five minutes away. The average response time for the first unit to arrive on the scene is less than four minutes. If a call originates from a nonparamedic ambulance district and a serious emergency or cardiac problem is suspected, the dispatcher notifies the ambulance unit closest to the scene of the reported incident and also the nearest paramedic ambulance unit.

Leaving Station

As the paramedic unit leaves the station on suspected cardiac runs, it contacts the coronary care unit at St. Paul-Ramsey Hospital by radio thus checking both radio and telemetry signal and notifying the coronary care unit nurse that a possible cardiac run is in progress. When the paramedic unit has arrived at the scene and ascertained that a cardiac run is indeed in progress, the coronary care unit nurse signals the in-hospital physician covering the unit by a paging system.

Arriving at Scene

Upon arrival at the scene, basic history, vital signs and pertinent physical examination are obtained by the paramedics and communicated to the physician at the hospital. If the emergency is cardiopulmonary in origin, they will continue to transmit voice and ECG signal to the coronary care unit. If however, it is a non-cardiac emergency, responsibility will be transferred by the CCU personnel to the emergency room where a physician responds. Therapy is directed by the physician in charge, whether it be in the coronary care unit or emergency room. When the patient is stabilized he is moved to the vehicle and transported to the hospital of his choice.

While operation of the multi-station system within the hospital is cumbersome, for us communications equipment in the coronary care unit and the emergency room has several advantages. It is easier to bring maximal expertise to bear on a given situation if equipment is contained in both places. Since many of the patients are transported to the emergency room for evaluation, they may monitor calls handled by the coronary care unit as well as be involved in initial transmission with other types of emergencies, thereby facilitating rapid patient care and disposition on arrival at the hospital. The disadvantage, of course, is increased cost of equipment and the possibility of misunderstanding who is primarily responsible for the patient. To avoid this confusion, assignment of responsibility must be clearly defined and only the physician directing care speaks to the paramedics.

For patients with acute myocardial infarction a major cause of delay in reaching the coronary care unit is time spent in emergency rooms that are ill-prepared to respond to acute cardiovascular emergencies. For this reason, direct admission of patients strongly suspected of having acute infarction, cardiac arrest or other serious rhythm disturbances to the coronary care units, especially in a community-wide system, using many hospitals, is desirable. A disadvantage of this system is that no physician has directly seen the patient prior to admission, but to date the hospitals in St. Paul have not found this to be a major problem.

Personnel

Paramedics continue to function as firefighters, as well, so that the emergency system has been implemented without the expenditure of additional funds for personnel. Each ambulance crew consists of four men, at least two of whom are trained paramedics. This, in our system, has been the minimum number necessary to manage a serious emergency. On a number of occasions, additional firefighters have been necessary to handle life-threatening emergencies.

Equipment

Equipment must be tailored to the method of operation suited to the individual community. Several vendors are available with some differences in methods. As with all medical equipment, selection must be partially based on availability of service. We feel the following key elements should be present:

1. Continuous ECG and simultaneous two-way voice radio communications with a multichannel capacity. There is some disagreement as to the need for continuous telemetry, but it does allow hospital personnel to continuously monitor the ECG signal. This is necessary because the paramedics may not always be able to see the oscilloscope.
2. Portable radio equipment must be small in size and light-weight with rapidly rechargeable batteries.
3. A mobile repeater in the ambulance ensures good portable site-to-base-station signal reception.
4. A system must provide for future expansion and interface with other existing emergency systems in the surrounding area.
5. A secondary telephone backup feature covers primary system failure.
6. The monitor-defibrillator should have as large a screen as possible for easy viewing. An ECG writer at the scene allows documentation of cardiac rhythm disturbances, accuracy of diagnosis and appropriateness of therapy should the radio/telemetry system fail.

Additional equipment such as the drug box, splints and other supplies on the ambulances require reserves in the fire station. Arrangements must be made at the hospital for replenishing supplies.

Costs

It is difficult to cost account any program which has depended on significant amounts of volunteer time to implement. Costs may be subdivided into: (a) equipment, (b) personnel, (c) training. Initial equipment purchases included monitor, defibrillator, ambulance radio equipment and base station equipment. Equipment must be selected which maximizes utilization of available personnel. Equipment costs may be amortized while personnel costs are ongoing. We feel duplicate CCU and ER equipment helps us achieve these ends.

A fulltime equivalent medical director was funded by the city/county government to coordinate the program as well as perform some instruction. It is impossible for one physician to have the varied background necessary to train this type of emergency personnel. In our case, a large cadre of medical and nursing specialists, mainly functioning as volunteers, donated significant amounts of time. Twenty-four hour a day medical and nursing coverage of the system must be considered. This may require augmentation of existing professional personnel.

Community Relations

A major feature in implementing a total community emergency service is recognition and input by community health care personnel. Early discussion and consideration of the needs of physicians within the community were solicited prior to implementation of this service by appearing before various medical groups to explain the project. This has made implementation easier and more satisfactory. To insure continued exchange of information, an advisory committee has been created with representation from most hospitals within the city. This has also enabled us to draw upon resources for teaching, criticism, and comment. Many day to day working problems arise and it is important that a mechanism exists for them to come to light and be solved.

Local government involvement, interest and enthusiasm are extremely important. In St. Paul, the support of the Mayor and the City/County government, enabled us to move through the usual bureaucracy in minimum time.

Many demonstrations of the paramedic system have been given by the St. Paul Fire Department in order to stimulate interest and facilitate utilization of the service. The community must be educated to this new type of service. It has been our experience that while reasonable exposure has been obtained by demonstrations and through the media, even more will be necessary to bring the system to full use.

Legality

Legislation to enable the paramedic personnel to perform this unique type of emergency medical care and offer legal protection to the paramedics and hospital personnel interacting with them must be considered. California and Washington have enacted legislation which is both enabling and protecting. Other communities have decided to operate under the broad protection offered by the Good Samaritan Act operative in that state. It was the opinion of the St. Paul City Attorney that the Good Samaritan Act in Minnesota was not sufficient to offer legal protection to the individuals working in this system. Therefore, a local Ramsey County Bill was passed by the state legislature in 1973 which permitted the practice of these skills learned by the paramedics, and offered protection under the utilization of reasonable care to the paramedic and hospital personnel.

The legislation specified certification by the State Board of Health after examination. The men trained to date have all been certified by the State Board of Health after examination and our program has been certified by them. It is our opinion that this legal protection is strongly advisable since this is a new type of service not previously available when the Good Samaritan Act in Minnesota was passed. Local legal opinion should be sought prior to implementation of this type of service, certainly in a community utilizing governmental personnel.

Early Operational Problems

Problems may be categorized into:

1. Equipment. A number of minor problems with integration of the total service arise once the equipment is installed. This makes local rapid service mandatory to avoid prolonged periods of down time. Certain problems are inherent in this type of system and might include:

a. Rough handling of equipment due to need for rapid mobility.

b. Build-up of outside dirt and moisture which accumulates quickly in electrical connections.

c. In addition, IV solutions have frozen quickly in Minnesota's rather frigid climate. This has not been a problem since its recognition but does limit starting IV's outside of the unit in cold weather.

2. Communications. The paramedical and hospital personnel must learn to communicate effectively and briefly. The success of the program is dependent upon a mutual respect between paramedical and medical personnel. A disadvantage of utilizing hospital residents is that they are available only for a limited time, in our case rotating every two to four months. Even given standardized types of instructions, there are difficulties since a real appreciation of the problems encountered is only gained through experience. The coronary care unit nurse who is a continuing hospital employee monitors each cardiac run along with the physician. Since she has ongoing experience there is continuity to the type of care rendered. Difficulties have been encountered in voice communications with interference occurring between various hospitals.

3. Continuing Education. This must be a part of any system. A hospital-based ambulance has an advantage in that men, during duty hours, are constantly available for re-training. A system with the units scattered throughout the city must include bringing the men back to the hospital for periodic retraining. Despite emphasis during both the initial training program and the continuing education, history and physical examination must be continually reinforced. This aspect is the most critical link in our chain of operations since without accurate data, optimal therapy is impossible.

4. Personnel Problems. These have been surprisingly few. The men work in crews on a rotational basis and soon learn to rely on each other. A consideration in the future may be the fatigue suffered by the men on the paramedic units. Since they also function as firefighters, they may be up continually during their twenty-four hour segment.

5. Education of the public is a continuing problem. Of the systems reviewed, Seattle seems to have had the most success because of a dedicated individual who constantly kept the paramedic service before the view of the public. This was done mainly through the newspaper and television media.

Summary

We have attempted to outline the implementing of an expanded emergency service which includes mobile coronary care. Each area defined has several alternatives depending upon community needs and resources. Program evaluation and constant updating must occur in order to obtain satisfactory results. A great deal of professional time is mandatory since the program must be closely observed by hospital and fire department officials. Continued feedback from the paramedics, from the community and consumers of the service is helpful. In general, we are satisfied with the early results of this program but recognize that continued education and improvement of service is mandatory.

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Request for Physician's Art Work

For many years the Board of Editors of Minnesota Medicine has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers have received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Pictures will be returned if identified with the name and address of the physician. Please submit your picture as prospective cover subjects to the Editor of Minnesota Medicine, 375 Jackson St., St. Paul, Minnesota 55101.

During 1976 the Editors would like to pay homage to the Bicentennial by having our covers depict places, events, objects, scenes, etc., that have historical or patriotic significance for the State of Minnesota. Please keep the Bicentennial theme in mind when submitting prospective covers for 1976.

Farrell Stiegler, M.D.
Cover Editor

Annual Meeting

A Meeting this great can only happen once a year!

Classified Advertisements

(Continued from page 108)

ONE OR TWO OB/GYN specialists wanted immediately for new, 120 bed hospital in Northern Wisconsin community of 10,000. Great water sports, fishing, and hunting abound in this Lake Superior vacation area. Good schools and new office space available adjacent to hospital. Contact: Kenneth Morrow, M.D., (715) 682-8146 after 7:00 p.m. or Lowell Miller (715) 682-4563.

LOCUM TENENS WANTED to work with three family physicians and a surgeon during January to July or portions thereof. Phone collect to Stuart Kaufman, M.D. or Wm. Dettweiler, Adm. (218) 834-2171. Community Clinic, Two Harbors, MN.

ASSOCIATION OR PARTNERSHIP DESIRED—35-year-old Family Practitioner in Southeastern Minnesota community (pop. 2000), 80 miles south of Twin Cities desires younger Family Physician 45 years old or less) to become associated in practice, leading to early partnership if interests mesh. Salary negotiable but in ball park. Hopefully interested, but necessarily tolerant of post graduate education, teaching medical students, time off for personal or family reasons and especially receptive to MEDEX or Physician's Assistant concept. Can guarantee only one night of primary call per week plus one Saturday and Sunday call per month, with the income benefits of only a 2-man group. High volume-high income practice in beautiful, recreational area of Minnesota. Please write or call: Timothy E. Nealy, M.D. Blooming Prairie, Minn. 55917. Phone (office) (507) 583-4415, (home) (507) 583-4400.

INTERNIST—Board eligible or certified, with or without sub-speciality interest, to join two busy Internists as an associate. Active medical community with drawing area of 100,000. New 130 bed JCAH hospital. Please mail C.V. to Philip H. Soucheray, M.D., 2101 Peaser Ave., Ashland, WI 54806, or call collect after 7:00 p.m.: John Kluge, M.D. (715) 682-4413.

FAIRMONT—FAMILY PRACTICE OR INTERNIST—Opportunity with multi-specialty clinic. Over the past four years the Fairmont Medical Clinic has added four new physicians to its staff. At the present time we are pursuing one additional man for the spring or summer, 1976. New clinic adjacent to a new 114-bed hospital in a rapidly growing community. Starting salary open, with early incentive, liberal time-off allowance and fringe benefits. Contact D. E. Grandgenett, Fairmont Medical Clinic, P.A. 56031 (507) 238-4263.

DOCTORS—THE NEXT MOVE IS YOURS—Midwest Medical, Inc. will provide you with more information about each opportunity than you have ever imagined possible. For the first time you can visually preview the Community and Medical Facilities of over 80 opportunities in the Upper Midwest, at ONE location. Saves you time, expense, and frustration. For a thorough appraisal of all factors involved, please accept our invitation to call. For discreet and confidential assistance contact M. A. Cornwall, M.D., MMI's Medical Director, or write: Midwest Medical, Inc., Lakeland, Minnesota 55043, 612-436-5161. Locum Tenens opportunities always available.

INTERNISTS to join progressive five-man group. Central Minnesota. 130 bed hospital. Lake area. Starting salary $40,000 per year. Fantastic practice opportunity. Contact Little Falls Clinic, Little Falls, Minnesota. 612-632-5305.

FAMILY PRACTITIONER—To join active, two-Doctor incorporated group practice in scenic Grantsburg, Wis. Salary open and negotiable. Modern clinic adjacent to 84 bed, JCAH Hospital. Excellent opportunity for MD out-door sports enthusiast. Fishing, hunting, skiing, snowmobiling, golf, and lakeshore living nearby. Cultural advantages of Twin Cities 75 freeway minutes away. Three of four weekends off plus one day off per week. Office affiliated with University of Wisconsin preceptorship program. Please contact: Richard L. Hartzell, M.D., Grantsburg Clinic, Ltd., Grantsburg, Wisconsin 54840. Phone: 715/463-5317.

UNIVERSITY OF MINNESOTA graduate, completing internship in June, 1976; seeking general practice situation in Wisconsin-Minnesota-Dakota area, solo or small group. Write: MINNESOTA MEDICINE-511, 101 E. 5th St., St. Paul 55101.

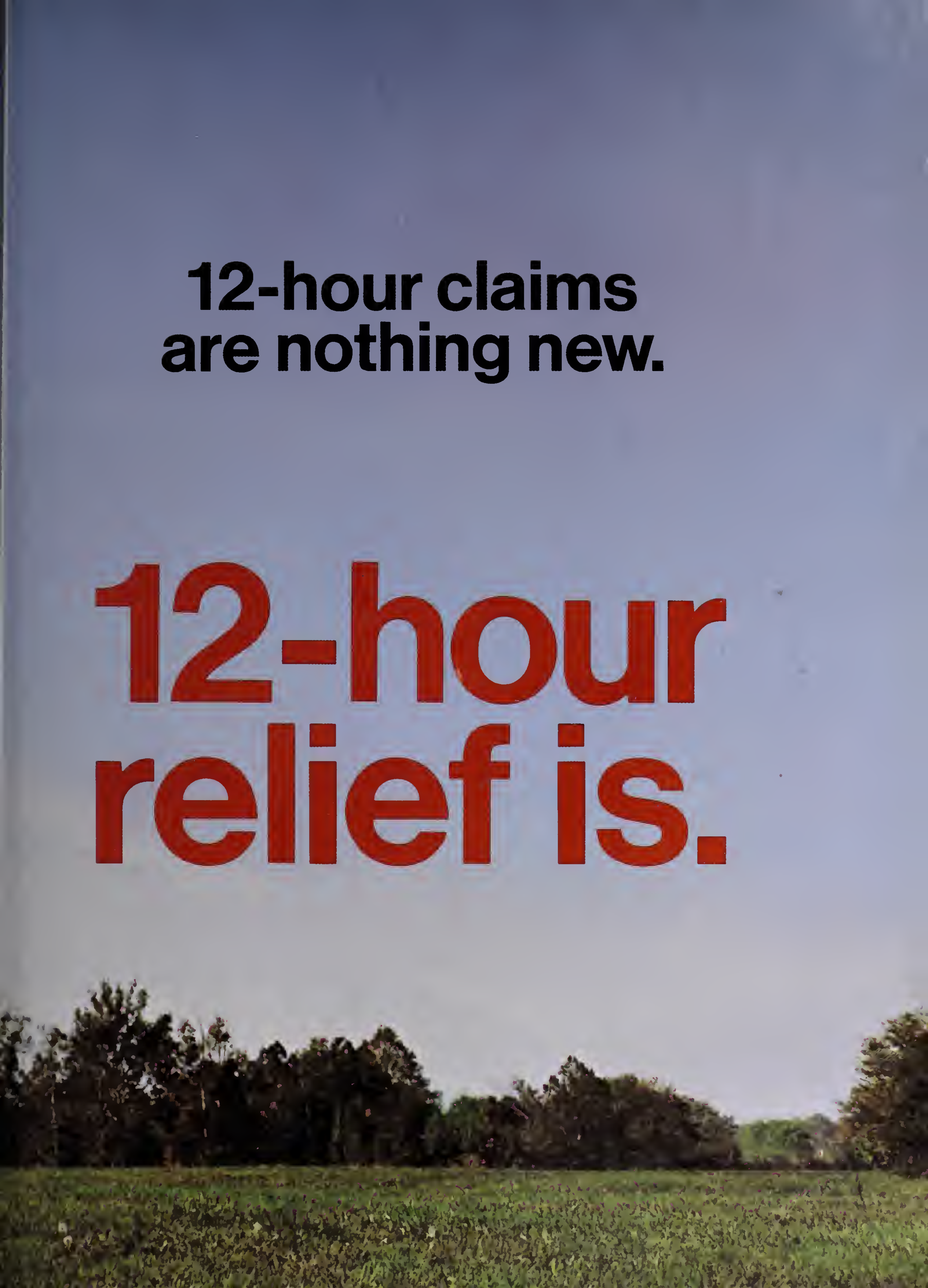
GENERAL PRACTITIONER to join MD in new Clinic in community of 2200; 25 miles southwest of Minneapolis; excellent schools and churches; productive farming area; 10-minute drive to hospital. Write or call Paul A. Stahler, M.D., Amo Vitae Clinic, 310 Sunset Drive, Jordan, Mn. 55352 612-492-6323.

FAMILY PHYSICIANS—MINNEAPOLIS. Opportunities for Board Certified or Board Eligible Family Practitioners in three neighborhood health centers of an 80-physician multi-specialty group. Present department consists of 7 Family Practitioners and a large Family Practice Residency Program. Please contact David J. Buran, M.D., St. Louis Park Medical Center, 5000 West 39th Street, Minneapolis, Minnesota 55416.

WANTED—Family practitioner, board eligible or board certified, to join 10-man multiple-specialty group with emphasis on family practice. Group now consists of seven family practitioners, one surgeon, one internist and two associates in OB-GYN. Located 30 miles west of Minneapolis, in brand new clinic facilities fully equipped for 12-man group next to 105-bed, fully accredited by JACH, designated area hospital. Contact J. W. Clarke, M.D. 448-2323.

PSYCHIATRY RESIDENCY: Vacancies for positions for those who have a regular Iowa License or can obtain one by reciprocity or via the FLEX. Prepare for career in private practice, community clinics or hospital based psychotherapy. Emphasis on close supervision of intensive individual and group psychotherapy, OPD, Children's Unit, Adolescent Unit. Neurology affiliation with University of Iowa. The Stipends are: 1st year, $20,280; 2nd year, $21,294; 3rd year, $22,360. Intensity and diversity of training program appreciated best by personal visit. Superintendent, Mental Health Institute, Cherokee, Iowa 51012. Equal Opportunity Employer. Call Collect 712-225-2594.

(Continued on page 142)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Each capsule contains pseudoephedrine hydrochloride 120 mg. and chlorpheniramine maleate 8 mg.

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It goes the distance.

Clinical studies confirm full 12-hour effectiveness.

For years, patients have heard of drugs providing long-lasting relief. But after six or eight hours, they often run out of relief. And it's too soon to take the next dose.

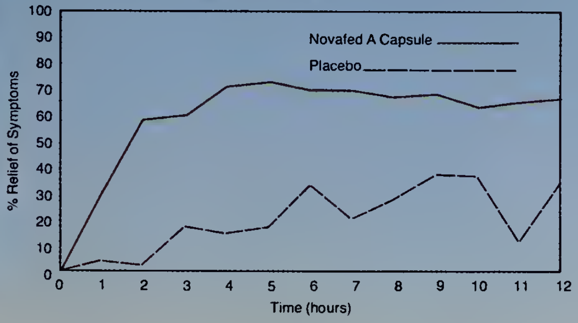
Now, with Novafed A, Dow introduces a prescription capsule with 12-hour effectiveness in relieving allergy and hay fever symptoms. Placebo-controlled clinical studies show that the high level of decongestant in Novafed A provides relief for as long as 12 hours. At the same time, its antihistamine relieves the patient's itchy eyes and runny nose *without* the excessive dryness of anticholinergic agents.

Prompt onset of effect is followed by full 12-hour relief.

(Please refer to the following page for bioavailability studies and prescribing information.)

Patients with severe pollen allergies were tested during hay fever season in a countryside environment and asked to rate severity of five different symptoms on a scale of 1 to 4.

Clinical Study: Degree of Relief from Itchy Eyes and Nose and Throat, Watery Eyes, Runny Nose*



*Unpublished data, Medical Department Files, Dow Pharmaceuticals, The Dow Chemical Company, Indianapolis, Indiana.

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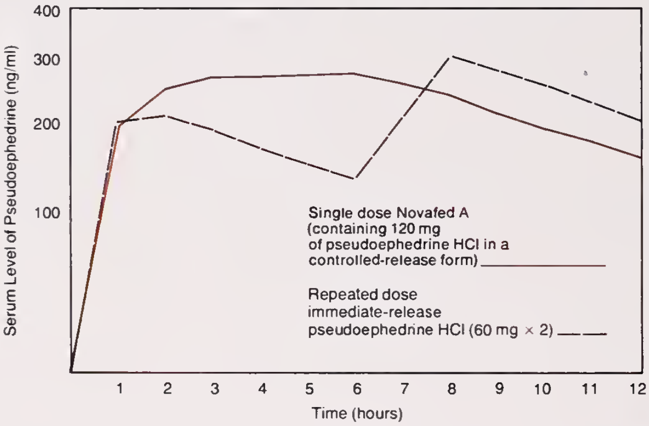
Prompt onset and sustained serum levels over 12 hours

A bioavailability study confirmed that the sustained 12-hour action of Novafed A was comparable to that of immediate-release medication taken at 6-hour intervals.

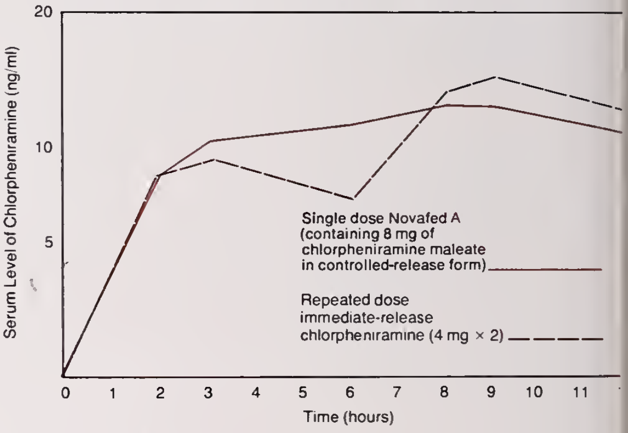
The chart at the left shows the serum levels of pseudoephedrine. Initial serum levels following one Novafed A Capsule were comparable to those following a single dose of 60 mg. pseudoephedrine hydrochloride in an immediate-release form. Serum levels of pseudoephedrine over a 12-hour period following a single dose of Novafed A were also comparable to those obtained by an immediate-release form taken every 6 hours.

The chart at the right shows the serum levels of chlorpheniramine. Initial serum levels following one Novafed A Capsule were comparable to those followin a single dose of 4 mg. chlorpheniramine maleate in an immediate-release form. Serum levels of chlorpheniramine over a 12-hour period following a single dose of Novafed A were also comparable to those obtained by an immediate-release form taken every 6 hours.

Comparison of Mean Serum Levels of Pseudoephedrine Following Novafed A and an Immediate-Release Reference Formulation*



Comparison of Mean Serum Levels of Chlorpheniramine Following Novafed A and an Immediate-Release Reference Formulation*



*Unpublished data, Medical Department Files, Dow Pharmaceuticals, The Dow Chemical Company, Indianapolis, Indiana.

DESCRIPTION: Each NOVAFEO A capsule contains 120 mg. of pseudoephedrine hydrochloride and 8 mg. of chlorpheniramine maleate. The specially formulated pellets in each capsule are designed to provide continuous therapeutic effect for about 12 hours. Nearly one-half of the active ingredients is released soon after administration and the remainder is released slowly over the remaining time period.

ACTIONS: NOVAFED A combines the action of a nasal decongestant, pseudoephedrine hydrochloride, and an antihistamine, chlorpheniramine maleate. These ingredients are combined to provide prompt and sustained nasal and upper respiratory decongestant and antihistaminic action.

INDICATIONS: NOVAFED A is indicated for the relief of nasal congestion and eustachian tube congestion associated with the common cold, sinusitis and acute upper respiratory infections. It is also indicated for perennial and seasonal allergic rhinitis, vasomotor rhinitis, allergic conjunctivitis due to inhalant allergens and foods and for mild, uncomplicated allergic skin manifestations of urticaria and angioedema. Decongestants in combination with antihistamines have been used for many years to relieve eustachian tube congestion associated with acute eustachian salpingitis, aerotitis media, acute otitis media and serous otitis media. NOVAFEO A may be given concurrently, when indicated, with analgesics and antibiotics.

CONTRAINDICATIONS: Symphathomimetic amines are contraindicated in patients with severe hypertension, severe coronary artery disease, and in patients on MAO inhibitor therapy. Antihistamines are contraindicated in patients with narrow-angle glaucoma, urinary retention, peptic ulcer, during an asthmatic attack, and in patients receiving MAO inhibitors.

Children under 12: NOVAFEO A controlled-release capsules should not be used in children less than 12 years of age.

Nursing Mothers: Pseudoephedrine is contraindicated in nursing mothers because of the higher than usual risk for infants from sympathomimetic amines.

Hypersensitivity: This drug is contraindicated in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines or antihistamines. Patient idiosyncrasy to adrenergic agents may be manifested by insomnia, dizziness, weakness, tremor or arrhythmias.

WARNINGS: Sympathomimetic amines should be used judiciously and sparingly in patients with hypertension, diabetes mellitus, ischemic heart disease, increased intraocular pressure, hyperthyroidism, or prostatic hypertrophy. Sympathomimetics may produce central nervous system stimulation and convulsions or cardiovascular collapse with accompanying hypotension.

Antihistamines may impair mental and physical abilities required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery, and mental alertness in children. Chlorpheniramine maleate has an atropine-like action and should be used with caution in patients with increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension or in patients with a history of bronchial asthma.

Do not exceed recommended dosage.

Use in Pregnancy: The safety of pseudoephedrine for use during pregnancy has not been established.

Use In Elderly: The elderly (60 years and older) are more likely to have adverse reaction to sympathomimetics. Overdosage of sympathomimetics in this age group may cause hallucinations, convulsions, CNS depression, and death. Therefore, safe use of a short-acting sympathomimetic should be demonstrated in the individual elderly patient before considering the use of a sustained-action formulation.

PRECAUTIONS: This drug should be used with caution in patients with diabetes, hypertension, cardiovascular disease and hyperreactivity to ephedrine. The antihistaminic may cause drowsiness and ambulatory patients who operate machinery or motor vehicles should be cautioned accordingly.

ADVERSE REACTIONS: Hyperreactive individuals may dis play ephedrine-like reactions such as tachycardia, palpit tions, headache, dizziness, or nausea. Patients sensitive to antihistamines may experience mild sedation.

Sympathomimetic drugs have been associated with certa untoward reactions including fear, anxiety, tenseness, restlessness, tremor, weakness, pallor, respiratory difficulty, dysuria, insomnia, hallucinations, convulsions, CN depression, arrhythmias, and cardiovascular collapse wit hypotension.

Possible side effects of antihistamines are drowsiness, restlessness, dizziness, weakness, dry mouth, anorexia, nausea, headache and nervousness, blurring of vision, heartburn, dysuria and very rarely, dermatitis.

DRUG INTERACTIONS: MAO inhibitors and beta adrenerg blockers increase the effect of sympathomimetics. Sympathomimetics may reduce the antihypertensive effects c methyldopa, mecamylamine, reserpine and veratrum alkaloids. Concomitant use of antihistamines with alcoh tricyclic antidepressants, barbiturates and other central nervous system depressants may have an additive effect.

DOSAGE AND ADMINISTRATION: One capsule every 12 hours. Do not give to children under 12 years of age.

CAUTION: Federal law prohibits dispensing without prescription.

HOW SUPPLIED: NOVAFED A is supplied in red and ora colored hard gelatin capsules, monogrammed with the Dow diamond followed by the number 109, in bottles of 100.

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Address

Our Political Responsibilities as Physicians

MATHIAS MASEM*

TODAY IT IS MY great honor and privilege to address this gathering upon the occasion of the recognition program in honor of our class. During the past four years we have been exposed to the most recent and advanced marvels of modern medicine. Indeed, we have been trained as medical scientists, the purveyors of modern medical technology, in a scientific tradition which has only recently elevated medicine from the realm of demonology to the age of organ transplantation.

Humanism

But we have also grown up at a time when science has seen its limitations. We have lived through perhaps the most tumultuous period in recent American history and witnessed the development of a radical political movement which rejected materialism and technological progress as its goal, and instead chose the pursuit of humanism and fundamental truth.

In support of Senator McCarthy's 1968 presidential candidacy, Erich Fromm stated in the "New York Times" that in a society in which "technological progress becomes the source of all values," the resulting consequence is "the complete alienation and dehumanization of man". The philosopher Herbert Marcuse crystalizes this idea in stating that "the mathematical character of modern science determines the range and direction of its creativity, and leaves the nonquantifiable qualities of "humanitas" outside the domain of exact science . . ." According to Mr. Marcuse, the reductionist thought process so central to the development of scientific knowledge clearly excludes ethical and moral considerations.

Medicine, An Art

As was so eloquently and succinctly stated by Dr. James Nelson, our commencement speaker of last year, the practice of medicine is an art. Such practice necessitates the role of artist, regarding the ethical and moral aspects of patient care as well as that of the artisan, with respect to the scientific and technical aspects.

Certainly moral and ethical concerns have not been neglected in the New Curriculum. Indeed, the tribulations of the course scheduling computer notwithstanding, and despite a daily mileage figure which might make us the most mobile medical student group in the history of medical education, we have acquired considerable expertise in the fields of death and dying and human sexuality and have been impressed by the compassionate and humanistic approach, beginning with our Student as Physician course, espoused by so many of our professors.

It is exactly because we have a considerable foundation as both artists and artisans in dealing with our humanistic as well as our scientific responsibilities that I would hope to approach another area of concern and address our political responsibilities as physicians.

Political Responsibility

The Federal Government is presently involved in health care to a major degree. This involvement could be generally divided into three categories: medical education, medical research, and health care services. Prior to the time of Abraham Flexner, most medical schools were proprietary. Following 1910, philanthropy became a major source of funding, with many of the big names in industry and finance, at that time, becoming involved. State governments also began to play a role through the State Universities but these funding sources became increasingly more resistant to subsidizing medical education when 50 percent of the medical graduates left their respective states. As the demands for funding increased, additional sources had to be sought and the rationale for federal participation in funding progressively increased. The Federal Government subsequently determined physicians to be a national resource and the Federal Health Professions Act of 1963 was passed.

Regarding medical research, it became clear in the 1930's that Dr. Hertzler in Kansas, and those like him, could no longer continue to work in sheds behind their homes. With a commitment to medical progress and improved health care, Congress enacted the legislation which established the National Institutes of Health. With considerable assistance from Mary Lasker and Florence Mahoney, who have been dubbed by Elizabeth Brenner Drew in "The Atlantic Monthly" as "Washington's Noble Conspirators", the NIH budget went from $2.5 million in 1945 to $1.4 billion in 1968 and presently supports greater than 40% of the biomedical research in this country.

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*President's Address to the Senior Class in Medicine, University of Minnesota, June 6, 1975.

Recently, however, the NIH has suffered a decline in its highly favored status and despite the efforts of the "noble conspirators", has felt a pinch for the first time in 40 years. The reason for this is that presently so much money is being paid for the provision of health care services that there is no longer so great an amount for NIH. Regarding basic research, Senator Edward Kennedy stated recently that the "informed consent of society was necessary to funding", with the inference that public expenditures ought to result from public decisions.

Finally, regarding health care services, the Federal Government began its involvement following World War II. At that time, increased demand for hospitals and health care services led to the enactment of the Hill-Burton Proposal. While significant in terms of its contribution, this act took on the proportions of a political football, leading to a remarkable proliferation of tiny hospitals in tiny towns, often not very far apart.

In 1965, Medicare and Medicaid were enacted and in 1966, at the recommendation of the DeBakey Committee, Regional Medical Program was enacted. This proposal had the specific objective of designating several regional centers at which the most recent scientific advances and achievements could be used in the treatment of cancer and heart and lung disease. If you will, it was an effort to bring NIH to the people.

In the meantime, the Medicare and Medicaid program began to have a profound effect on the health care system. The increased demand secondary to increased purchasing power led to a cost escalation and the present 17 percent annual rate of expansion of hospital services, with the rate of expansion of physicians' services somewhat below that. A striking example of this effect can be seen in the annual number of physicians going into practice. In 1963, 6000 Medical Doctors were graduated and this year 15,000 of us will graduate and 15,000 more foreign physicians will be licensed to practice.

That is quite a change and it seems reasonable to expect that the Federal Government might then move to determine just what proportion of the national resources, i.e. the GNP, ought to be devoted to health, and then to begin planning for the more efficient and effective allocation and utilization of a limited commodity.

Such considerations led to the amendment of the Social Security Act in 1972, establishing the Physicians Standard Review Organization or PSRO. The Foundation for Health Care Evaluation is such an organization, functioning here in Minneapolis and is responsible for the utilization review reports we have all seen on patients' charts informing us that, for example 90% of patients with the diagnosis of "myocardial infarction", within a certain period have been discharged. The PSRO legislation specifically addresses the premise that most health costs originate with the physician, and attempts to limit them. The legislation provides for the assumption of responsibility by some physician group in the review of medical care of all federal beneficiaries. This is to assure that the care delivered is necessary and of high quality, and to eliminate some amount of unnecessary health services.

In 1973 the Health Maintenance Organization Act was passed. This measure was intended to provide funding in order to encourage the growth of HMO's but the benefits, such as open enrollment, predisposed to adverse selection which has proven to be generally discouraging. There is presently an amendment being drafted.

In 1974, the Health Planning and Resources Development Act, authored by Rep. Bill Roy, a physician from Topeka, Kansas, was enacted. This measure provided for the establishment of geographically and demographically defined health planning regions within each state. Each will be governed by a board of consumers as well as providers and will be charged with the determination of health needs as well as a plan for that region. The boards will further be charged with a review of existing facilities and rationalization of health services according to the needs of the region. This proposal does not include a grandfather clause so that even established physicians' services will be subject to review. This type of administration is essentially a public utility model by which providers are franchised by the health governing boards, which would be somewhat analogous to the public school boards.

With what I have said as background, I believe the implications of the new health care system should be considered. There should be little argument among us that our scientific and technical expertise and sophistication has reached such a degree that we do not have the resources to provide all of the benefits of modern health science to everyone everywhere. In addition, the health care expenditures for over a decade have been rising at a rate of twice that of the rate of growth of the GNP and considerably more rapidly than the rate of growth of the economy. Present health care expenditures represent 8 percent of the GNP and there is certainly some question how much greater an expenditure can be tolerated.

Both PSRO and CHP work in conjunction, toward the most efficient use and the allocation of a limited resource. While such an attempt at rationing might not immediately seem appealing it should be noted that rationing of health care services presently exists, but in a non-system which functions from discrepancies in availability, accessibility, and education. I believe an organized approach with established priorities and medical expertise would be remarkably superior, and likewise would be certainly superior to rationing done on purely a fiscal basis, as in Phase 4 controls, under which services and fees could increase only a given amount.

Health Manpower Legislation

Additionally, we might expect health manpower legislation in the near future which will address the problem of geographic and specialty maldistribution. It does not seem likely with the magnitude of federal funding in medical education that Congress will long tolerate the concentrations of physicians on either coast and in the suburbs nor be able to afford the luxury of a situation as in Massachusetts where there are as many neurosurgeons, with a population of 5 million people, as there are in England and Wales, with a population of 50 million people. Under this legislation, areas of geographic and specialty need will be identified and physicians and other health professionals will be trained and designated to meet that need.

Finally, we can anticipate that PSRO, CHP, and Health Manpower will provide the matrix upon which universal third party payment, or in other words, national health insurance can be instituted. However this need not be done with public monies and there is considerable justification for the use of private carriers, in terms of their flexibility and efficiency.

Presently, in the context of current and impending health legislation, we should hardly need to be reminded of our political responsibilities. According to Don Price, Dean of the John F. Kennedy School of Government at Harvard, "many scientists are still inclined to think that the moral obligation of a scientist is to remain aloof from policy issues and political controversy." Yet the day has come when all of our scientific expertise and ethical principles will be viewed in the light of cost effectiveness. As Dr. William Fifer would say, "let us keep the health in HEW" and indeed the consequences would constitute a disastrous compromise, in allowing uninformed welfare administrators to determine health policy.

We are the future of medicine in this country and we will be following a book of rules for practice in the new health care system which has not yet been written. But we can help shape those rules. While we can not all be legislators, we can all remain informed. While we can not all draft laws, we can remain responsive. And it is incumbent upon us to assure that health policy never poses a compromise to the quality of our health care.

References can be obtained from Mathias Masem, 616 Moraga St., #3, San Francisco, CA. 94122

Pediatric Conferences—Children's Hospital St. Paul

These conferences have been approved by the American Academy of Family Practice for Continuing Education and are held the second and fourth Thursdays from 8:30 to 9:30 a.m. in the Auditorium.

February 12	"A Perspective on Pediatrics of Yesteryear"	Robert Rosenthal, M.D.
February 26	"Recent Work in Perinatal Adrenal Function"	John W. Reynolds, M.D.

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For more than thirty years PREMARIN (Conjugated Estrogens Tablets, U.S.P.) has been prepared with natural equine estrogens exclusively—without synthetic estrogen supplements. For more than thirty years it has provided the complete estrogen complex in the proportions found in its natural source. And for more than thirty years PREMARIN has enjoyed an unparalleled record of clinical efficacy and acceptance.

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Indications: Based on a review of PREMARIN Tablets by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications for use as follows:
Effective: As replacement therapy for naturally occurring or surgically induced estrogen deficiency states associated with: the climacteric, including the menopausal syndrome and postmenopause; senile vaginitis and kraurosis vulvae, with or without pruritus.
"Probably" effective: For estrogen deficiency-induced osteoporosis, and only when used in conjunction with other important therapeutic measures such as diet, calcium, physiotherapy, and good general health-promoting measures. Final classification of this indication requires further investigation.

Contraindications: Short acting estrogens are contraindicated in patients with (1) markedly impaired liver function; (2) known or suspected carcinoma of the breast, except those cases of progressing disease not amenable to surgery or irradiation occurring in women who are at least 5 years postmenopausal; (3) known or suspected estrogen-dependent neoplasia, such as carcinoma of the endometrium; (4) thromboembolic disorders, thrombophlebitis, cerebral embolism, or in patients with a past history of these conditions; (5) undiagnosed abnormal genital bleeding.
Warnings: Estrogen therapy should not be given to women with recurrent chronic mastitis or abnormal mammograms except, if in the opinion of the physician, it is warranted despite the possibility of aggravation of the mastitis or stimulation of undiagnosed estrogen-dependent neoplasia.

The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, retinal thrombosis, cerebral embolism and pulmonary embolism). If these occur or are suspected, estrogen therapy should be discontinued immediately.

Estrogens may be excreted in the mother's milk and an estrogenic effect upon the infant has been described. The long range effect on the nursing infant cannot be determined at this time.

Hypercalcemia may occur in as many as 15 percent of breast cancer patients with metastases, and this usually indicates progression of bone metastases. This occurrence depends neither on dose nor on immobilization. In the presence of progression of the cancer or hypercalcemia, estrogen administration should be stopped.

A statistically significant association has been reported between maternal ingestion of diethylstilbestrol during pregnancy and the occurrence of vaginal carcinoma in the offspring. This occurred with the use of diethylstilbestrol for the treatment of threatened abortion or high risk pregnancies. Whether or not such an association is applicable to all estrogens is not known at this time. In view of this finding, however, the use of any estrogen in pregnancy is not recommended.

Failure to control abnormal uterine bleeding or unexpected recurrence is an indication for curettage.

Precautions: As with all short acting estrogens, the following precautions should be observed:

A complete pretreatment physical examination should be performed with special reference to pelvic and breast examinations.

To avoid prolonged stimulation of the endometrium and breasts in climacteric or hypogonadal women, estrogens should be administered cyclically (3 week regimen with 1 week rest period—withdrawal bleeding may occur during rest period).

Because of individual variation in endogenous estrogen production, relative overdosage may occur which could cause undesirable effects such as abnormal or excessive uterine bleeding, mastodynia and edema.

Because of salt and water retention associated with estrogenic anabolic activity, estrogens should be used with caution in patients with epilepsy, migraine, asthma, cardiac, or renal disease.

If unexplained or excessive vaginal bleeding should occur, reexamination should be made for organic pathology.

Pre-existing uterine fibromyomata may increase in size while using estrogens; therefore, patients should be examined at regular intervals while receiving estrogenic therapy.

The pathologist should be advised of estrogen therapy when relevant specimens are submitted.

Because of their effects on epiphyseal closure, estrogens should be used judiciously in young patients in whom bone growth is incomplete.

Prolonged high dosages of estrogens will inhibit anterior pituitary functions. This should be borne in mind when treating patients in whom fertility is desired.

The age of the patient constitutes no absolute limiting factor, although treatment with estrogens may mask the onset of the climacteric.

Certain liver and endocrine function tests may be affected by exogenous estrogen administration. If test results are abnormal in a patient taking estrogen, they should be repeated after estrogen has been withdrawn for one cycle.

Adverse Reactions: The following adverse reactions have been reported associated with short acting estrogen administration:
nausea, vomiting, anorexia
gastrointestinal symptoms such as abdominal cramps and bloating
breakthrough bleeding, spotting, unusually heavy withdrawal bleeding (See DOSAGE AND ADMINISTRATION)
breast tenderness and enlargement
reactivation of endometriosis
possible diminution of lactation when given immediately postpartum
loss of libido and gynecomastia in males
edema
aggravation of migraine headaches
change in body weight (increase, decrease)
headache
allergic rash
hepatic cutaneous porphyria becoming manifest

Dosage and Administration: PREMARIN should be administered cyclically (3 weeks of daily estrogen and 1 week off) for all indications except selected cases of carcinoma and prevention of postpartum breast engorgement.

Menopausal Syndrome—1.25 mg. daily, cyclically. Adjust dosage upward or downward according to severity of symptoms and response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control.

If the patient has not menstruated within the last two months or more, cyclic administration is started arbitrarily. If the patient is menstruating, cyclic administration is started on day 5 of bleeding. If breakthrough bleeding (bleeding or spotting during estrogen therapy) occurs, increase estrogen dosage as needed to stop bleeding. In the following cycle, employ the dosage level used to stop breakthrough bleeding in the previous cycle. In subsequent cycles, the estrogen dosage is gradually reduced to the lowest level which will maintain the patient symptom-free.

Postmenopause—as a protective measure against estrogen deficiency-induced degenerative changes (*e.g.* osteoporosis, atrophic vaginitis, kraurosis vulvae)—0.3 mg. to 1.25 mg. daily and cyclically. Adjust dosage to lowest effective level.

Osteoporosis (to retard progression)—usual dosage 1.25 mg. daily and cyclically.

Senile Vaginitis, Kraurosis Vulvae with or without Pruritus—0.3 mg. to 1.25 mg. or more daily, depending upon the tissue response of the individual patient. Administer cyclically.

How Supplied: PREMARIN (Conjugated Estrogens Tablets, U.S.P.)

No. 865—Each *purple* tablet contains 2.5 mg., in bottles of 100 and 1,000.

No. 866—Each *yellow* tablet contains 1.25 mg., in bottles of 100 and 1,000. Also in unit dose package of 100.

No. 867—Each *red* tablet contains 0.625 mg., in bottles of 100 and 1,000.

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BRAND OF CONJUGATED ESTROGENS TABLETS, U.S.P.

CONTAINS ONLY NATURAL ESTROGENS ...NO SYNTHETICS OR SUPPLEMENTS

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AYERST LABORATORIES
New York, N.Y. 10017

Testing in Humans: Who, Where & When.

the weight of ethical opinion:

Few would disagree that the effectiveness and safety of any therapeutic agent or device must be determined through clinical research.

But now the *practice* of clinical research is under appraisal by Congress, the press and the general public. Who shall administer it? On whom are the products to be tested? Under what circumstances? And how shall results be evaluated and utilized?

The Pharmaceutical Manufacturers Association represents firms that are significantly engaged in the discovery and development of new medicines, medical devices and diagnostic products. Clinical research is essential to their efforts. Consequently, PMA formulated positions which it submitted on July 11, 1975, to the Subcommittee on Health of the Senate Labor and Public Welfare Committee, as its official policy recommendations. Here are the essentials of PMA's current thinking in this vital area.

1. PMA supports the mandate and mission of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and offers to establish a special committee composed of experts of appropriate disciplines familiar with the industry's research methodology to volunteer its service to the Commission.

2. PMA supports the formation of an independent, expert, broadly based and representative panel to assess the current state of drug innovation and the impact upon it of existing laws, regulations and procedures.

3. When FDA proposes regulations, it should prepare and publish in the *Federal Register* a detailed statement assessing the impact of those regulations on drug and device innovation.

4. PMA proposes that an appropriately qualified medical organization be encouraged to undertake a comprehensive study of the optimum roles and responsibilities of the sponsor and physician when company-sponsored clinical research is performed by independent clinical investigators.

5. PMA recognizes that the physician-investigator has, and should have, the ultimate responsibility for deciding the substance and form of the informed consent to be obtained. However, PMA recommends that the sponsor of the experiment aid the investigator in discharging this important responsibility by providing (1) a document detailing the investigator's responsibilities under FDA regulations with regard to patient consent, and (2) a written description of the relevant facts about the investigational item to be studied, in comprehensible lay language.

6. In the case of children, the sponsor must require that informed consent be obtained from a legally appropriate representative of the participant. Voluntary consent of an older child, who may be capable of understanding, in addition to that of a parent, guardian or other legally responsible person, is advisable. Safety of the drug or device shall have been assessed in adult populations prior to use in children.

7. PMA endorses the general principle that, in the case of the mentally infirm, consent should be sought from both an understanding subject and from a parent or guardian, or in their absence, another legally responsible person.

8. Pharmaceutical manufacturers sponsoring investigations in prisons must take all reasonable care to assure that the facilities and personnel used in the conduct of the investigations are suitable for the protection of participants, and for the avoidance of coercion, with a respect for basic humanitarian principles.

9. Sponsors intending to conduct non-therapeutic clinical trials through the participation of employee volunteers should expand the membership and scope of its existing Medical Research Committee, or establish such an internal Medical Research Committee, with responsibility to approve the consent forms of all volunteers, designs, protocols and the scope of the trial. The Committee should also bear responsibility to ensure full compliance with all procedures intended to protect employee volunteers' rights.

10. Where the sponsor obtains medical information or data on individuals, it shall be accorded the same confidential status as provided in codes of ethics governing health care professionals.

11. PMA and its member firms accept responsibility to aid and encourage appropriate follow-up of human subjects who have received investigational products that cause latent toxicity in animals or, during their use in clinical investigation, are found to cause unexpected and serious adverse effects.

12. PMA supports the exploration and development by its member companies of more systematic surveillance procedures for newly marketed products.

13. When a pharmaceutical manufacturer concludes, on the basis of early clinical trials of a basic new agent, that a new drug application is likely to be submitted, a proposed development plan accompanied by a summary of existing data, would be submitted to the FDA. Following a review of this submission, the FDA, and its Advisory Committee where appropriate, would meet with the sponsor to discuss the development plan. No *formal* FDA approval should be required at this stage. Rather, the emphasis should be on identification of potential problems and questions for the sponsor's further study and resolution as the program develops.

The PMA believes that health professionals as well as the public at large should be made aware of these 13 points in its Policy on Clinical Research. For these recommendations envisage constructive, cooperative action by industry, research institutions, the health professions and government to encourage creative and workable responses to issues involved in the clinical investigation of new products.

P·M·A

Pharmaceutical Manufacturers
Association
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(Continued from page 130)

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STUDENT HEALTH SERVICE, Director, Mankato State University. Located in South Central Minnesota: on Campus enrollment of 10,000 students; metropolitan area of 50,000; current Minnesota license necessary. Salary competitive, five-day work week, liberal vacation, and fringe benefits. Contact Karen Delesha, Administrative Director, Student Health Service, Mankato State University, Mankato, Minnesota 56001, phone (507) 389-2726. Equal Opportunity/Affirmative Action Employer.

FAMILY PRACTITIONER needed to join other GP at the Pine City Clinic. New Clinic facilities including lab and x-ray. Excellent opportunity for rapid growth. Contact Oskar P. Friedlieb, M.D., 307 First Street North, Virginia, Minnesota 55792 or Ruel Martinson, M.D., Pine City Clinic, Pine City, Minnesota 55063.

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(potassium chloride)
ELIXIR
10%

DESCRIPTION:
Each 15 ml. (tablespoonful) contains:
Potassium Chloride ....1.5 g.
(supplying 20 meq.)
Alcohol 4%
in a palatable base. Contains no sugar.

KAY CIEL®
(potassium chloride)
POWDER
Solodose®

DESCRIPTION:
Each *Solodose* packet contains:
Potassium Chloride ....1.5 g.
(supplying 20 meq.)
flavored. Contains no sugar.

INDICATIONS: Treatment and prevention of potassium deficiency occurring especially during thiazide diuretic or corticosteroid therapy, digitalis intoxication, low dietary intake of potassium, or as a result of excessive vomiting and diarrhea and for correction of associated hypochloremic alkalosis.

CONTRAINDICATIONS: Impaired renal function, untreated Addison's Disease, dehydration, heat cramps and hyperkalemia.

WARNINGS: Do not use excessively.

PRECAUTIONS: Administer with caution and adjust to the requirements of the individual patient. The patient should be checked frequently and periodic ECG and/or plasma potassium levels made. Use with caution in patients with cardiac disease. In hypokalemic states, attention should be directed toward the correction of the frequently associated hypochloremic alkalosis. ***Patients should be cautioned to adhere to dilution instructions.***

ADVERSE REACTIONS: Potassium intoxication indicated by listlessness, mental confusion, paresthesia of the extremities, weakness of the legs, flaccid paralysis, fall in blood pressure, cardiac depression, arrhythmias, arrest and heartblock. Vomiting, nausea, abdominal discomfort and diarrhea may occur.

DOSAGE AND ADMINISTRATION: *Elixir:* One tablespoonful (15 ml. supplying 20 meq.) **diluted** in 4 ounces of water or fruit juice twice daily (preferably after a meal), or as directed by physician. *Powder:* Contents of 1 packet dissolved in 4 ounces of water or fruit juice twice daily (preferably after a meal), or as directed by physician.

OVERDOSAGE: In case of excessive use resulting in hyperkalemia or potassium intoxication, discontinue use of potassium chloride administration or take other steps to lower serum levels if indicated.

HOW SUPPLIED: *Elixir:* In bottles of: 473 ml. (16 fl. oz.) ...NDC 0041-0143-16. 3785 ml. (128 fl. oz.)...NDC 0041-0143-28. *Powder:* In boxes of: 30 *Solodose* packets...NDC 0041-0144-30.

143-38R/COS-878

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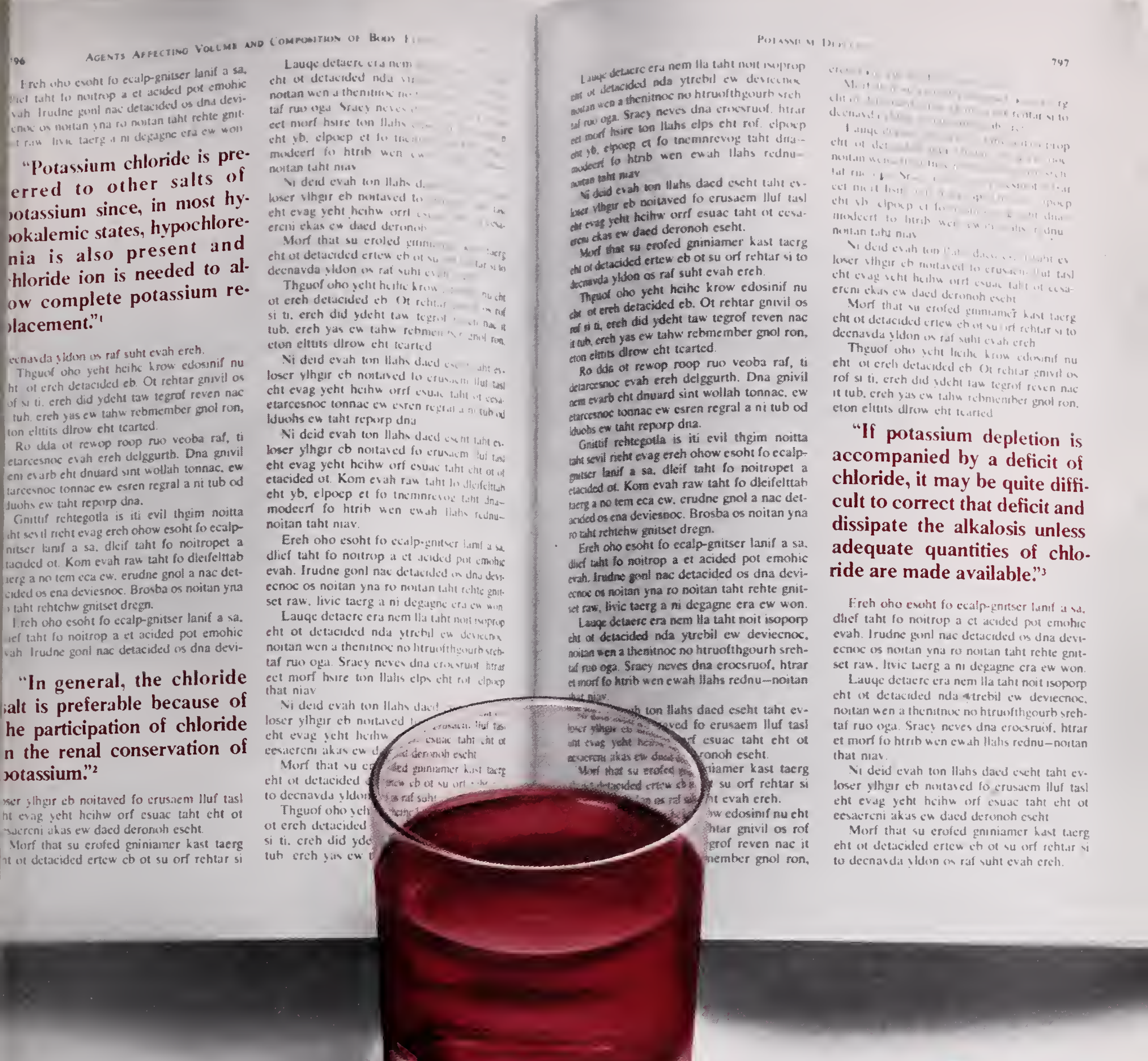
Cooper Laboratories, Inc.
Wayne, New Jersey 07470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Agents Affecting Volume and Composition of Body F
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“Potassium chloride is pre-
erred to other salts of
otassium since, in most hy-
okalemic states, hypochlore-
nia is also present and
hloride ion is needed to al-
ow complete potassium re-
lacement.”[1]
“In general, the chloride
alt is preferable because of
he participation of chloride
n the renal conservation of
otassium.”[2]
“If potassium depletion is
accompanied by a deficit of
chloride, it may be quite diffi-
cult to correct that deficit and
dissipate the alkalosis unless
adequate quantities of chlo-
ride are made available.”[3]

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KAY CIEL® Powder
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1. AMA Drug Evaluations, ed. 2, Publishing Sciences Group, Inc., Acton, Mass., 1973, p. 184.
2. Sandstead, H., in Wintrobe, M.M. *et al.* (Eds.): Harrison's Principles of Internal Medicine, ed. 7, New York, McGraw-Hill Book Company, 1974, p. 441
3. Welt, L.G., in Goodman, L.S., and Gilman, A. (Eds.): The Pharmacological Basis of Therapeutics, ed. 4, New York, The Macmillan Company, 1970, pp. 798-799.

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Index to Advertisers

Allied Medical Audit Control, Inc. 144
American Medical Association 119
Anderson, C. F., Co. 112
Ayerst Laboratories 138, 139
Burroughs-Wellcome Co. 70
Classified Advertising 108
Cooper Laboratories, Inc. 142, 143
Dahlberg Hearing Aids 68
Dow Pharmaceuticals 131, 132, 133, 134
Finley & Friday, Inc. 98
Flint Laboratories 75, 76, 120, 121, 122
Kjell Bergh's Borton Volvo, Inc. 72
Lilly, Eli, & Co. 78
Medcalf Orthopedic Appliance Co. 144
Medical Protective Company 72
Merck Sharp & Dohme 90, 91, 92
Pharmaceutical Mfrs. Assn. 140, 141
Robins, A. H., Co. 109, 110, 111
Roche Laboratories .... Cover 2, 67, 102, 103, 104, Covers 3-4
Roerig and Company 89
Smith, Kline & French 101
Trautmans 112
Volvo, Kjell Bergh's Borton 72
Western Life Insurance Company 112

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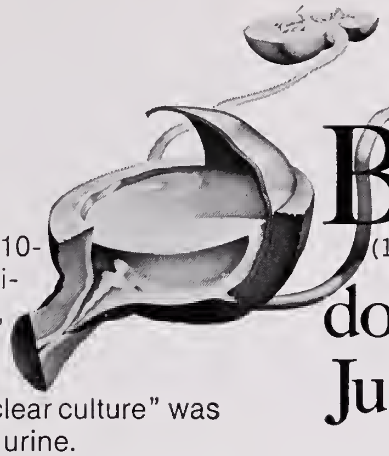
1020 LaSalle Ave., Minneapolis, Minn. 55403 332-5391

10-day Bactrim therapy
utperforms 10-day ampicillin therapy.



In a multicenter, double-lind study of patients with hronic or frequently recurrent rinary tract infection, Bactrim 10-ay therapy outperformed ampi-illin 10-day therapy by 27.2%, hen comparing patients ho maintained clear cultures r eight weeks. Criterion for "clear culture" was 000 or fewer organisms/ml of urine.

Vhile adverse reactions were mild (*e.g.*, nausea, ash), more serious reactions can occur with these rugs. See manufacturers' product information r complete listing.

ote: Bactrim single strength tablets were used in these clinical ials. However, studies have established the bioequivalency of actrim DS with the single strength tablets.

Bactrim™ DS
(160 mg trimethoprim and 800 mg sulfamethoxazole)
double strength tablets
Just 1 tablet B.I.D.

Bactrim™
(80 mg trimethoprim and 400 mg sulfamethoxazole)
2 tablets B.I.D.

For chronic or frequently recurrent cystitis and pyelonephritis due to susceptible organisms.

efore prescribing, please consult complete product information, a ummary of which follows:

ndications: Chronic urinary tract infections evidenced by persistent acteriuria (symptomatic or asymptomatic), frequently recurrent infec-ions (relapse or reinfection), or infections associated with urinary ract complications, such as obstruction. Primarily for cystitis, pyelo-ephritis or pyelitis due to susceptible strains of *E. coli*, *Klebsiella-nterobacter*, *Proteus mirabilis*, *Proteus vulgaris* and *Proteus organii.*

OTE: The increasing frequency of resistant organisms limits the use-ulness of antibacterials, especially in these urinary tract infections.

he recommended quantitative disc susceptibility method (*Federal egister, 37*:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to tri-methoprim-sulfamethoxazole" indicates an infection likely to respond o Bactrim therapy. If infection is confined to the urine, "Intermedi-ate susceptibility" also indicates a likely response. "Resistant" indi-cates that response is unlikely.

ontraindications: Hypersensitivity to trimethoprim or sulfonamides; regnancy; nursing mothers.

arnings: Deaths from hypersensitivity reactions, agranulocytosis, plastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been re-ported as well as an increased incidence of thrombopenia with pur-pura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **Data are insufficient to recommend use in in-fants and children under 12.**

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase defi-ciency, hemolysis, frequently dose-related, may occur. During ther-apy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, par-ticularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimeth-oprim are included, even if not reported with Bactrim. *Blood dys-crasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypopro-thrombinemia and methemoglobinemia. *Allergic reactions:* erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfolia-tive dermatitis, anaphylactoid reactions, periorbital edema, con-junctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomati-tis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pan-creatitis. *CNS reactions:* Headache, peripheral neuritis, mental de-pression, convulsions, ataxia, hallucinations, tinnitus, vertigo, in-somnia, apathy, fatigue, muscle weakness and nervousness. *Miscel-laneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to cer-tain chemical similarities to some goitrogens, diuretics (acetazola-mide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglyce-mia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dos-age: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) every 24 hours
Below 15	Use not recommended

Supplied: Double Strength (DS) tablets, each containing 160 mg tri-methoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10.

Oral suspension, containing in each teaspoonful (5 ml) the equiva-lent of 40 mg trimethoprim and 200 mg sulfamethoxazole; fruit-licorice flavored—bottles of 16 oz (1 pint).

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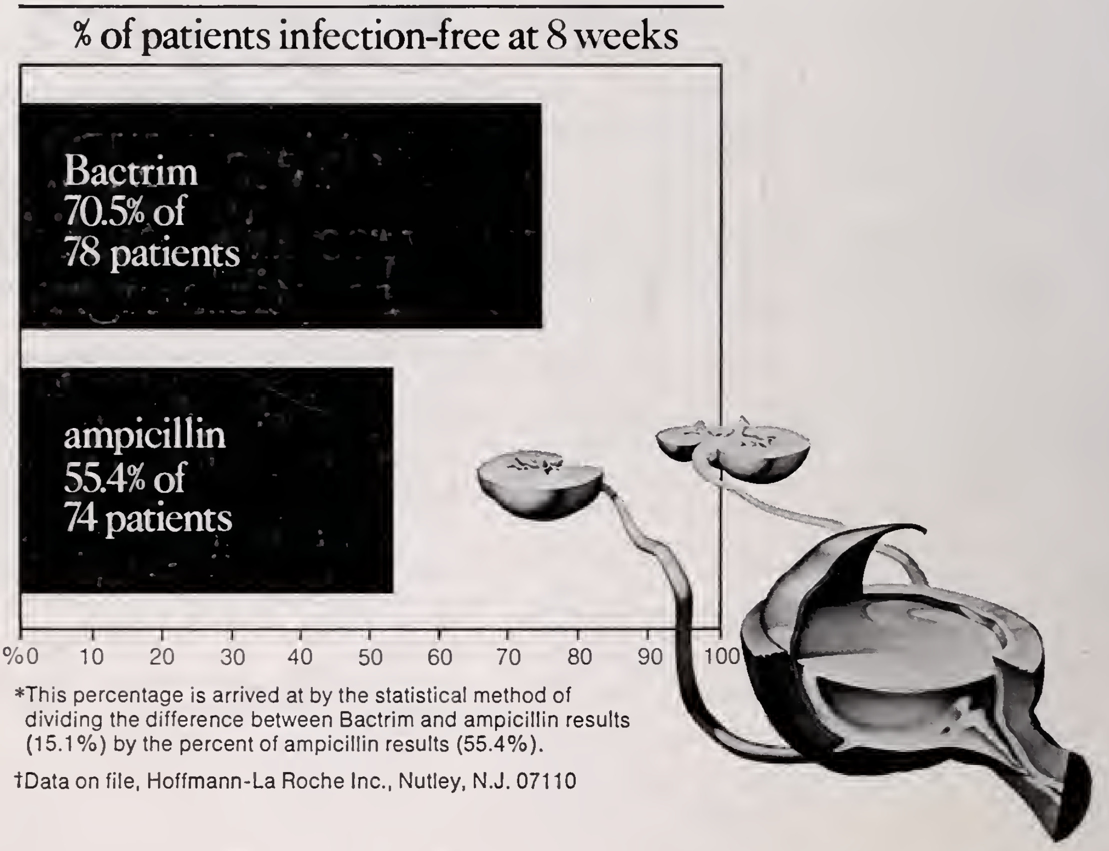
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

In a multicenter study of patients with chronic or frequently recurrent urinary tract infections

Library College of Physicians/s
19 So. 22nd St.
Philadelphia, PA 19103

Bactrim T.M. was 27.2%* more effective than ampicillin in keeping patients infection-free for 8 weeks.†



*This percentage is arrived at by the statistical method of dividing the difference between Bactrim and ampicillin results (15.1%) by the percent of ampicillin results (55.4%).

†Data on file, Hoffmann-La Roche Inc., Nutley, N.J. 07110

Bactrim T.M. DS

(160 mg trimethoprim and 800 mg sulfamethoxazole)
double strength tablets
Just 1 tablet B.I.D.

Bactrim T.M.

(80 mg trimethoprim and 400 mg sulfamethoxazole)
2 tablets B.I.D.

Please see summary of product information on preceding page.

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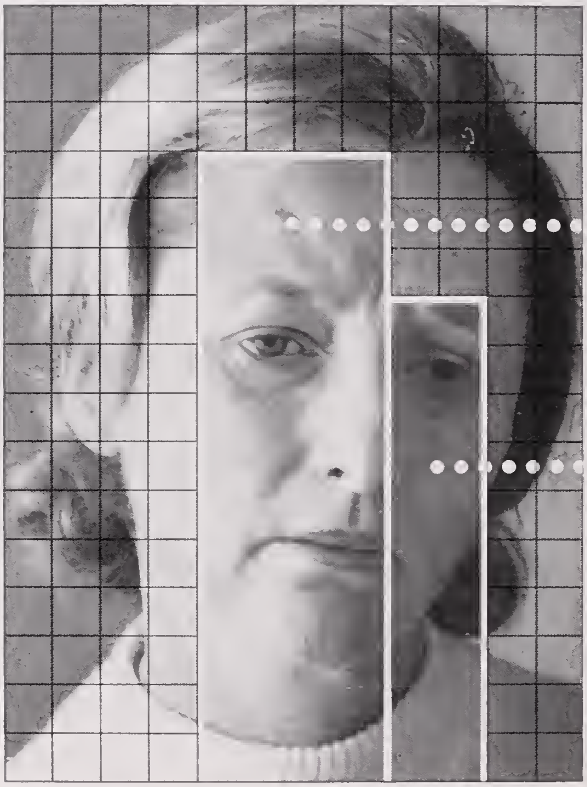

Predominant psychoneurotic anxiety

Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in fr
and/or severity of grand mal seizu s
require increased dosage of stand
convulsant medication; abrupt wit
may be associated with temporary
crease in frequency and/or severi of
seizures. Advise against simultane s
gestion of alcohol and other CNS d
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provide relief for both—as
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associated with it are also
relieved.
There are other advan-
s in using Valium for the
agement of psychoneu-
anxiety with secondary
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im is pronounced and
d. This means that im-
ement is usually apparent

in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

Valium®
(diazepam) (IV)
2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

illance because of their predisposi-
o habituation and dependence. In
nancy, lactation or women of child-
ng age, weigh potential benefit
ist possible hazard.
utions: If combined with other psy-
opics or anticonvulsants, consider
ully pharmacology of agents em-
d; drugs such as phenothiazines,
otics, barbiturates, MAO inhibitors
other antidepressants may potentiate
tion. Usual precautions indicated in
nts severely depressed, or with latent
ession, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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President's Letter

The FTC

The Federal Trade Commission (FTC) has issued a complaint against the American Medical Association charging the AMA with restraining competition by preventing physicians from advertising. Can you believe it? The professionalism of medicine is at stake. The public, our patients, must be informed of the deleterious effects of this action—an action taken without public hearings and without prior discussion or consultation with the medical profession. The foundation of the code of medical ethics developed and adopted by the profession after years of study and debate is being attacked supposedly in the defense and support of consumerism.

In the proceedings initiated by the FTC, the Connecticut State Medical Society and the New Haven County Medical Association, for reasons that are not clear, are also named as respondents. The complaint asks for an order which would require the parties named to "stop taking any action which interferes with the right of an individual physician to advertise his services or to otherwise engage in open and free competition with other doctors." It is alleged that the principles of medical ethics of the AMA prevents members from advertising types and prices of their services thereby lessening competition, fixing and stabilizing prices, and denying consumers the opportunity to obtain the information they need to select a physician.

Could any action against medicine be more damaging to the consumers (our patients) whom the FTC seeks to protect. The FTC has to answer some very pertinent questions: (1) What is the evidence that the code of ethics against advertising restricts competition and fixes and stabilizes prices (fees)? (2) How does restriction on advertising in any way deny our patients the opportunity to select the physician of their choice? (3) Is the hucksterism of advertising professional medical services with all its excesses which were found to be unacceptable to the profession and the public in the past, now to be regarded as acceptable? (4) When all other agencies of government are seeking to curb the excesses in advertising, can the FTC claim credibility by attacking a professional code of ethics that has convincingly protected the consumer from these excesses?

Can there be any better proof of the success of this code of medical ethics than the esteem in which our patients hold us? Every major poll, each reported widely, is available to demonstrate the FTC action was unwarranted.

GRDiessner

G. Roy Diessner M.D.
President
Minnesota State Medical Association

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Editor's Notebook

Editor's Note: The Minneapolis Star and certain radio stations picked up last month's weather editorial on Minnesota's glories and Florida's miseries and saw fit to bring this news to the general public's attention. Because of the glare and heat of the publicity, my thoughts on other subjects have temporarily dried up. I have consulted minny, the literary cockroach who doubles as Minnesota Medicine's mascot, about this problem. He offered here the following piece of advice.

when your tank runs low

dear boss
the wordsmith game
has its ups and downs
when you are up
your tank runs over
but when you are down
the tank runs low
if you try
to fill the tank
by force
pressure just
stirs up
the bottom
your tank you see insists
on making its own gas
but if you feed and drink
upon the wise words
that others wrote
your tank will
absorb and digest
and synthesize
the words into
inner thoughts
that sooner or later
will spill over the top
but even better yet
if you just leave
your tank alone
it will become
an artesian well
and fill
itself

minny

RLR

Minnesota State Medical Association

Annual Meeting

The Importance of Being Ticketed . . .

The importance of being ticketed has nearly obsessed some of this year's Annual Meeting planners. Wondering why this was so, I considered the question of tickets and realized that one can not attend the theater, a football game, or enter a parking ramp without a ticket. You need a ticket to pick up your shirts at the laundry, board a commercial airplane, or ascend a ski slope. And in 1976, you can't even "run" without a ticket! So, it probably comes as no surprise that you will not be admitted to any of the CME '76 scientific program without a ticket.

The reasons for ticketing are many. Besides offering proof of your seminar registration, tickets provide means by which you can evaluate content, presentation methods, and overall effectiveness of seminars. (They also reserve you seating space and assure restricted attendance in restricted attendance sessions!). You will be showing your tickets at the door of each seminar. Keep the ticket with you during the session, then, complete the five or six brief questions on its reverse side, and drop it into the evaluation receptacle as you leave.

There are twelve seminars in this year's program, six different seminars presented morning and afternoon on Thursday and Friday, each seminar's attendance limited by the size of the physical facilities in which it is presented. Since seminar room capacities range from 100 to 150, you will be assured of optimal audio and visual facilities in an uncrowded learning atmosphere.

If you register early, your chances of getting your first choices in seminars are excellent. Registration materials will be on their way to you in early March, and we encourage you to choose the seminars you wish to attend and return this information to the State Office with your registration fee as soon as possible. The preregistration deadline is May 12. Also make certain that your registration fee ($10 for members, $25 for non-members) accompanies your seminar selections, because registrations received without fees will not be processed. No fee is required for residents, interns, and medical students. Registration material packets including seminar tickets can be picked up at the registration desk by those who have preregistered. Those who have not preregistered will find themselves waiting in line while their foresighted colleagues sit comfortably in seminars. MSMA staff and Scientific Assembly Subcommittee members will be on hand to help last minute registrants select from the scientific programs not yet filled.

Because you laid the groundwork for the scientific sessions when you filled out evaluation cards last May, *CME '76* is able to present educational opportunities that correspond to the majority's requests. The meeting will offer enjoyable social activities and constructive business sessions too, and you are cordially invited to attend and enjoy every facet of *Chirurgical and Medical Emergencies '76 (CME '76)*. Register for the meeting as early as possible . . . remember, preregistration is your ticket to the Association's most important event of the year!

R. D. Semsch, M.D.
Chairman
Scientific Assembly

Natural balance
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Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

nd useful in the management of vertigo* associated with es affecting the vestibular system.

relieve nausea and vomiting often associated with vertigo.*

al adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.

available as Antivert (meclizine HCl) 12.5 mg. scored s, for dosage convenience and flexibility.

ivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for a, vomiting and dizziness associated with motion sickness.

UMMARY OF PRESCRIBING INFORMATION

ICATIONS. Based on a review of this drug by the National Academy of ces—National Research Council and/or other information, FDA has classified dications as follows:

ective: Management of nausea and vomiting and dizziness associated with n sickness.

sibly Effective: Management of vertigo associated with diseases affecting the ular system.

al classification of the less than effective indications requires further tigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

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FOR LONG-TERM CONTROL OF HYPERTENSION*

Serum K+ and BUN should be checked periodically. (See Warnings Section.)

SPARES POTASSIUM

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

> * **Warning**
> This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematolo studies in cirrhotics with splenomegaly. A hypertensive effects may be enhanced in pc sympathectomy patients. The following n occur: hyperuricemia and gout, reversible nitro retention, decreasing alkali reserve with poss metabolic acidosis, hyperglycemia and glycos (diabetic insulin requirements may be alter digitalis intoxication (in hypokalemia). cautiously in surgical patients. Concomitant with antihypertensive agents may result in additive hypotensive effect. 'Dyazide' interf with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakn dizziness, headache, dry mouth; anaphyla rash, urticaria, photosensitivity, purpura, o dermatological conditions; nausea and vomi (may indicate electrolyte imbalance), diarr constipation, other gastrointestinal disturban Necrotizing vasculitis, paresthesias, icte pancreatitis, xanthopsia and, rarely, alle pneumonitis have occurred with thiazides al

Supplied: Bottles of 100 capsules; in Single Packages of 100 (intended for institutional only).

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Contents—March, 1976

OVER PHOTOGRAPH—"Minnesota at Gettysburg"
Julien V. Petit, M.D. 181

RESIDENT'S LETTER—The FTC
G. Roy Diessner, M.D., President 149

DITOR'S NOTEBOOK—when your tank runs low
minny 151

RIGINAL CONTRIBUTIONS

Atherosclerotic Coronary-Artery Aneurysms
Ronald Olin, M.D. et al. 157

Thrombophlebitis
Claus A. Pierach, M.D. et al. 164

Intravenous Hydrochloric Acid in the Treatment of Metabolic Alkalosis
Robert A. Petzel, M.D. et al. 166

DITORIALS

Transverse Myelopathy in Heroin Addiction
John M. McKelvey, M.D. 175

Two Primary Intracranial Tumors
Joo Ho Sung, M.D. 177

Intractable Ascites
Harrison H. Farley, M.D. 177

Treatment of Metabolic Alkalosis with Intravenous Hydrochloric Acid
Donald A. Duncan, M.D. 179

LETTERS TO THE EDITOR

George Friedell, M.D. 180
Joel T. M. Bamford, M.D. 180

GONORRHEA SCREENING IN OLMSTED COUNTY DURING 1974
G. R. Pettersen, M.D. and Lyle A. Weed, M.D. 169

RAMSEY COUNTY MEDICAL SOCIETY—What's Right with Medicine?
Thomas G. Briggs, M.D., Society President 183

MINNESOTA STATE MEDICAL ASSOCIATION—Annual Meeting
R. D. Semsch, M.D., Chairman Scientific Assembly 152

SCAN CONFERENCE—Dryness of Mouth and Eyes
S. H. Tsai, M.D. 185

REVIEW—Transfusion Review in Minnesota Hospitals
John O. Swanson, M.D. and Herbert F. Polesky, M.D. 188

LABORATORY MEDICINE—Should You Add PEP to Your Office Lab?
Richard M. Steidl, M.D. 191

SPECIAL ARTICLE—The Philosophy of Preventive Medicine
John E. Smith, M.D. 196

RURAL PHYSICIAN ASSOCIATES—An Information Service for Rural Physician Associate Program Students
Gertrude Foreman et al. 200

PUBLIC HEALTH NURSING—Adult/Geriatric Nurse Practitioners in Minnesota
Eva Anderson Vraspir, R.N. et al. 203

CONTINUING MEDICAL EDUCATION 170, 181, 192, 205, 210

IN MEMORIAM 206

BOOK REVIEW 207

CLASSIFIED ADVERTISEMENTS 208

INDEX TO ADVERTISERS 210

Volume 59, No. 3
Pages 145-210

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Atherosclerotic Coronary-Artery Aneurysms

Report of Five Cases Diagnosed by Cine-Coronary Arteriography

RONALD OLIN, M.D.,* DAVID L. DUVAL, M.D.* and D. NEIL DICKSON, M.D.*

Five cases of Atherosclerotic Aneurysms of the Coronary Arteries are presented. All were diagnosed during life by cine coronary arteriography and occurred in 1.8 per cent of such arteriograms done over a two year period. Review of the literature including the classification and pathogenesis of coronary aneurysms is also presented.

SINCE THE FIRST description of a coronary-artery aneurysm by Bougon in 1812[1], just over 100 cases have been reported in the literature, almost all being diagnosed at postmortem. About 50% of cases were due to atherosclerosis, the commonest cause. Since coronary arteriography was first introduced in 1952[2], four cases[3-6] have been diagnosed during life. Munkner et al. in 1958[3] reported the first aneurysm recognized by this method. This was a congenital coronary aneurysm in an eight-year-old child.

Over a two-year period from November, 1971, to December, 1973, 273 cine-coronary arteriograms were performed at St. Luke's Hospital, Fargo, North Dakota, with the finding of five cases of coronary-artery aneurysms, all atherosclerotic in type.

This report presents these five cases and briefly reviews the subject of coronary-artery aneurysms.

Case Reports

Case 1

A 57-year-old housewife was referred on March 22, 1972, for cine-coronary arteriography. In 1963, a subtotal thyroidectomy for a nontoxic goiter was done elsewhere and she had been taking thyroid, three grains daily. In 1968, a routine electrocardiogram (ECG) showed nonspecific repolarization abnormalities and an exercise ECG was positive. She denied any symptoms suggestive of coronary-artery disease. Menopause had occurred at age 50. She smoked about a third of a package of cigarettes daily.

Physical examination was unremarkable. The blood pressure was 135/85 and the pulse normal.

Laboratory tests revealed the following: Hb 15.4 gm.%; WBC 6,200 with a normal differential; normal urinalysis; FBS 100 mg.% (our normal 70-110 mg.%); cholesterol 337 mg.% (our normal 150-280 mg.%); triglycerides 221 mg.% (our normal 50-200 mg.%); and BUN 15.4 mg.%. Chest Xray was negative. A 12-lead ECG was abnormal with ST-segment depression in II, III, AVF, V_4 to V_6.

A right femoral artery percutaneous puncture was done with selected catheterizations of the right and left coronary arteries and a ventriculogram. In the anterior descending branch of the left coronary artery, there was a 7 mm. aneurysm arising just prior to the division of the diagonal branch (Figures 1A and B). There was about 50% atherosclerotic narrowing proximal to the aneurysm for a short distance; just distal to the aneurysm, there was further 60-70% narrowing over a 1.5 cm. distance. The aneurysm was not calcified and contained no filling defects. The left circumflex and right coronary arteries showed extensive calcific atherosclerosis with 60%-80% narrowing. The ventriculogram showed that the left ventricle contracted to about half its normal size with mild hypokinesis but no definite areas of akinesis.

She was seen again in September, 1972, and March, 1973, and felt well, denying angina. Serum cholesterol was 288 and 282 mg.%, respectively, on these occasions.

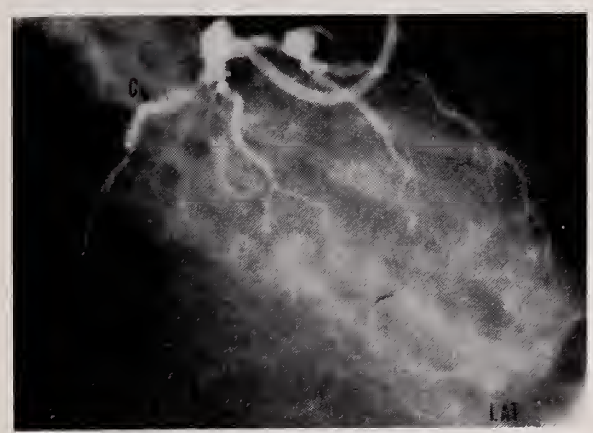

Fig. 1(A)—Case 1; Left coronary-artery injection, lateral view, shows, 7-8 mm. saccular aneurysm in the LAD branch. The left circumflex artery (C) shows extensive plaque formation with about 60% narrowing at its origin.

---

*Departments of Internal Medicine, Cardiovascular Disease and Radiology, Fargo Clinic, Box 2067, Fargo, N.D.

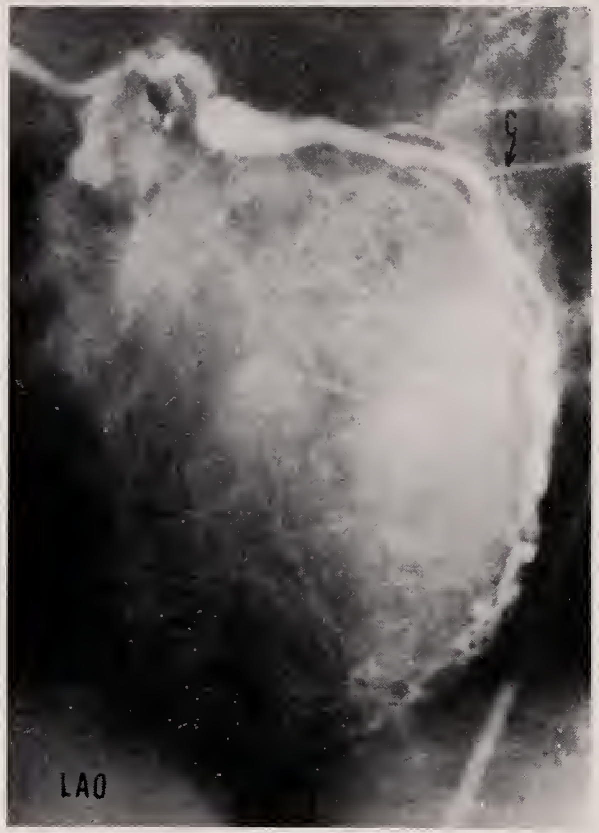

Fig. 1(B)—Case 1; Left coronary-artery injection, left anterior oblique view, again shows aneurysm in LAD branch.

Case 2

A 62-year-old housewife was referred on January 16, 1973, for cardiac evaluation. There was no history of acute rheumatic fever. An uncomplicated myocardial infarction had occurred in 1966. For one year, she had noted progressive effort angina. In June of 1972, she was hospitalized for one week in congestive heart failure. She was taking Lanoxin, Inderal, Isordil, Dyazide and Thyroid.

Physical examination revealed a height of 62 inches, weight 92 lbs., blood pressure 110/60 and an irregular pulse at 80-90 beats per minute. Jugular venous pressure appeared normal and the lungs were clear. Cardiac examination revealed a left ventricular quick thrust, irregular rhythm with a ventricular rate of 90, an accentuated second pulmonic sound, a Grade 2 (basis 1-6) apical blowing pansystolic murmur and a mild diastolic rumble and a grade 2 decrescendo blowing early diastolic murmur along the left sternal border.

Laboratory tests revealed the following: Hb 15 gm.%; WBC 6,500; sed. rate 27 mm, per hour; FBS 97 mg.%; cholesterol 292 mg.%; triglycerides 176 mg.%; total thyroxin 7.1 mcg.%; BUN 36 mg.% and essentially normal urinalysis. Chest Xray with cardiac fluoroscopy demonstrated moderate cardiomegaly primarily of the left atrium, left and right ventricles; there was dense calcification of the mitral valve area and probably also in the aortic valve; there was also definite calcification in the left coronary artery as well as the right coronary artery as far as the apex. A 12-lead ECG showed atrial fibrillation with a ventricular rate of 70, poor progression

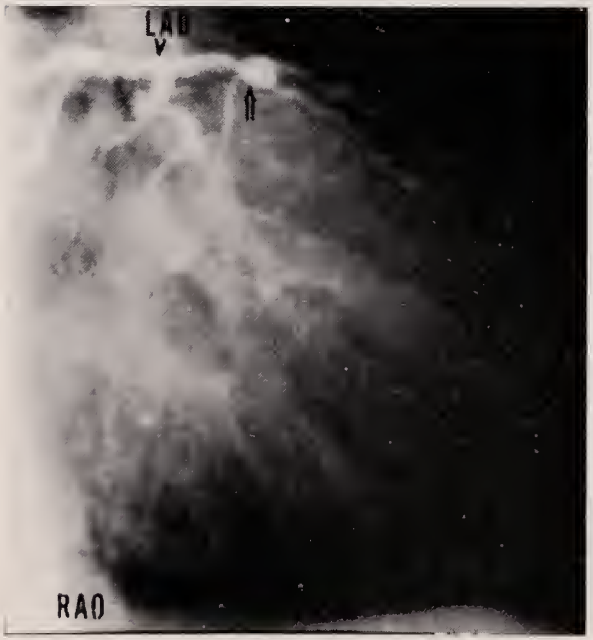

Fig. 2(A)—Case 2; Left coronary-artery injection, right anterior oblique view, shows LAD branch completely occluded at its origin and an 11-12 mm. fusiform aneurysm in the left circumflex artery.

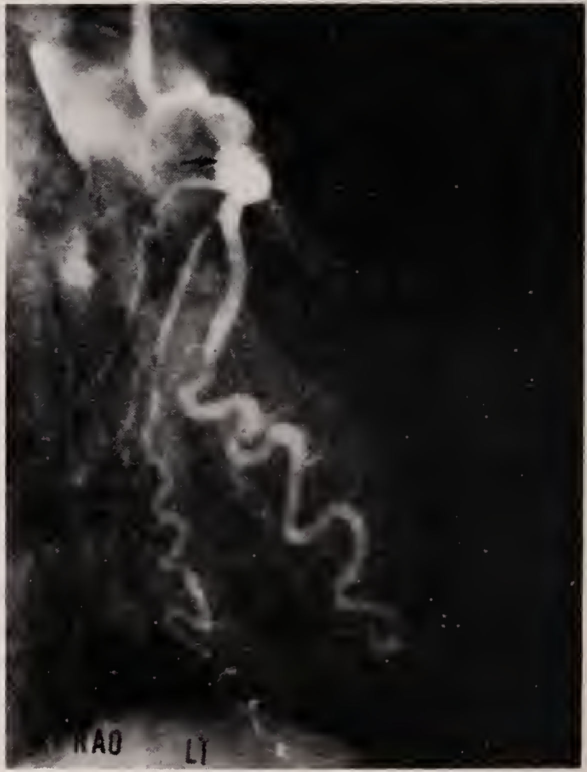

Fig. 2(B)—Case 2; another view of the aneurysm in the left circumflex artery.

of the R-wave in V_1 to V_3 suggesting an old anteroseptal scar, low voltage in the limb leads and sagging S-T segments in II, V_4 to V_6. The clinical impression was coronary-artery disease with an old anteroseptal myocardial infarction and rheumatic heart disease with mitral stenosis and insufficiency, and aortic insufficiency (Class III).

Right and left cardiac catheterization and cine-coronary arteriography were done via the right basilic vein to the right heart and the right femoral artery to the left heart and coronary arteries. Coronary arteriography revealed severe coronary artery disease with the anterior descending branch of the left coronary artery completely occluded at its origin; there was no collateral flow from either the left circumflex branch or right coronary arteries. The left circumflex branch was 90% narrowed about 1-2 cm. distal to its origin with an 11-12 mm. fusiform aneurysm just beyond (Figures 2A and B). The right coronary artery showed spotty disease throughout with no major areas of narrowing. None of the distal nonvisualized arteries filled via collaterals. The ventriculogram showed sluggish ventricular action with no areas of specific flattening. There was a severe mitral stenosis with an estimated valve area of 0.52 cm.^{2} and 2+ mitral regurgitation.

Because of severe triple vessel coronary-artery disease and the obvious need for mitral valve replacement, the operative risk was thought to be prohibitive in the order of 50% or more. It was decided to continue with a conservative medical program. She expired at home on September 13, 1973, from a presumed massive myocardial infarction. Autopsy was not done.

Case 3

A 32-year-old housewife was referred for cardiac evaluation on June 19, 1972. She had an acute inferior myocardial infarction six months previously and since then was experiencing sharp left upper chest pains radiating down the left arm brought on by emotion. Her father had died at age 50 from a coronary thrombosis. A brother had a coronary thrombosis at age 26, was still living, documented by coronary angiography. Two sisters ages 27 and 28 were known to have hypercholesterolemia. She smoked a half to one package of cigarettes daily and was taking Atromid-S.

Physical examination revealed a height of 62 inches, weight 110 lbs., blood pressure 110/70 and normal pulse. There was a grade 1 short mid systolic murmur at the lower left sternal border to the apex.

Laboratory tests revealed the following: Hb 13.9 gm%; WBC 5,600; FBS 90 mg.%; cholesterol 344 mg.%; triglycerides 80 mg.% and normal urinalysis. Lipoprotein electrophoresis revealed a type II abnormality. Chest Xray was negative. An ECG showed Q-waves in III, AVF and diphasic T-waves in AVF. A cine-coronary arteriogram revealed two vessel disease and a coronary artery aneurysm. She was advised to discontinue tobacco, additional medications were suggested, and she was followed until October 1, 1973, when she returned to relate that she was having more chest and arm pains. Serum cholesterol was 480 mg.%. A Holter ECG recording for 24 hours was negative. A stress exercise ECG was positive.

A repeat cine-coronary arteriogram on October 9, 1973, revealed normal left main coronary and left circumflex arteries. There was a 1 cm. in length aneurysmal dilatation in the proximal left anterior descending branch protruding 5 mm. just prior to the origin of the diagonal branch (Figure 3). There was about 80% narrowing just distal to the aneurysm for a short segment before the origin of the diagonal branch. The diagonal branch also had 50% stenosis proximally. The distal left anterior descending branch was not remarkable. The right coronary artery showed about an 80% narrowing over a 5-6 mm. distance arising just after the origin of the right ventricular branch. Distally the right artery was normal with three or four descending branches. The SA nodal artery and the AV nodal arteries were demonstrated arising from the right. There was no collateral circulation. The left ventricular end-diastolic pressure was elevated to 20 mm. Hg. The ventriculogram showed that the ventricle was more dilated than previously with a definite area of paradoxical pulsation of the proximal one-half of the left ventricular wall and hypokinesis of the distal one-half of the anterior wall and distal two-thirds of the posterior wall. Diastolic emptying was only moderate.

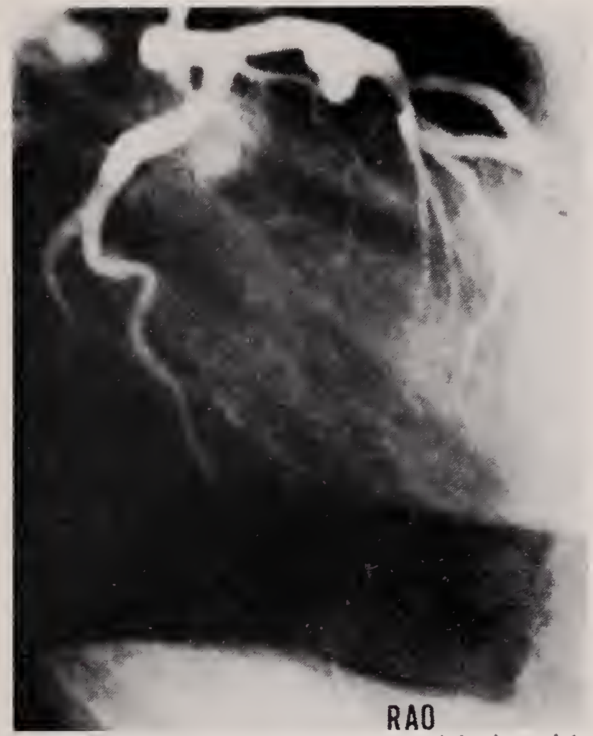

Fig. 3—Case 3; Left coronary-artery injection, right anterior oblique view, shows 1 cm. aneurysmal dilatation in the proximal LAD branch just prior to the origin of the diagonal branch.

On October 13, 1973, under extracorporeal circulation, two saphenous vein grafts were inserted from the aorta to the distal right coronary artery and left anterior descending branch. Recovery was uneventful.

When seen as an outpatient on December 12, 1973, she was doing well and having no angina.

Case 4

A 51-year-old housewife and nurse was referred on September 4, 1972, for cardiac evaluation. Toxemia had been present with all four pregnancies and hypertension since the first pregnancy 20 years ago. She had been taking HydroDiuril and Valium. In April, 1972, she was hospitalized elsewhere for six weeks with a myocardial infarction. In August, 1972, she was hospitalized again because of a syncopal episode and chest pains. An ECG showed initially that the T-waves were inverted but these became upright. Since that time, she was experiencing eight to ten anginal episodes a day, rarely at rest (class III). She was taking Isordil, Inderal and Valium.

Physical examination revealed a height of 64 inches, weight of 144 lbs., b.p. 124/80 and normal pulse. The remainder of the examination was not remarkable.

Laboratory tests revealed the following: Hb 14.7 gm%; WBC 5,400; ESR 9 mm./hr; FBS 100 mg.%; cholesterol 333 mg.%; triglycerides 140 mg.% and normal serum K+, BUN and urinalysis. Chest Xray was normal. A 12-lead EKG showed ST segment depression in I, II, V_5 and V_6. A Holter EKG scan for 24 hours revealed ST-segment depression at 3:00 p.m. compatible with ischemia; the only rhythm disturbance was a sinus tachycardia.

On September 11, 1972, a cine-coronary arteriogram was done which showed that the left coronary artery was dominant. There was 80-90% narrowing of the left anterior descending branch after it gave rise to the second of two large diagonal branches. There was a 1 cm., saccular aneurysm without clot formation at the point of narrowing (Figure 4A). Distal to this, the left anterior descending branch was tortuous but uninvolved. The origin of the left circumflex artery had a 70% narrowing over a distance of 1 cm. with minor atherosclerotic changes beyond but no significant narrowing. The right coronary artery was almost completely occluded distally after it gave rise to the marginal branch. The visualized portion showed extensive saccular aneurysmal deformities particularly the proximal several cms (Figure 4B). There was no collateral circulation. The ventriculogram was normal.

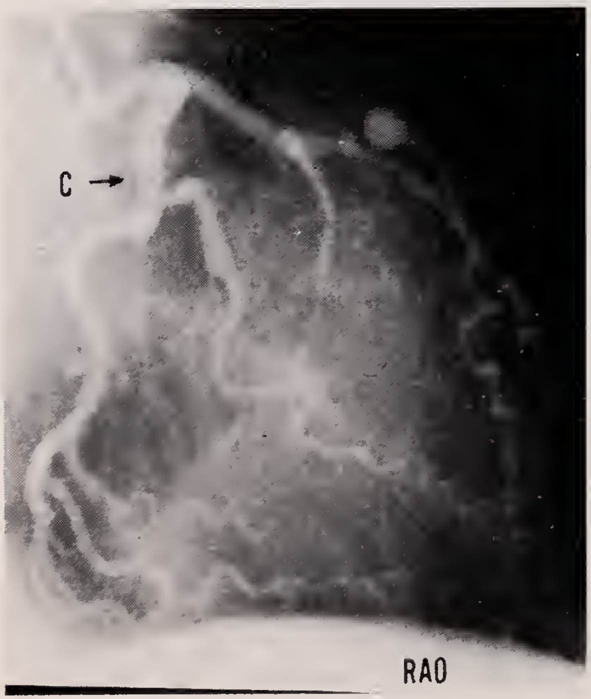

Fig. 4(A)—Case 4; Left coronary-artery injection, right anterior oblique view, shows 1 cm. saccular aneurysm in the LAD branch.

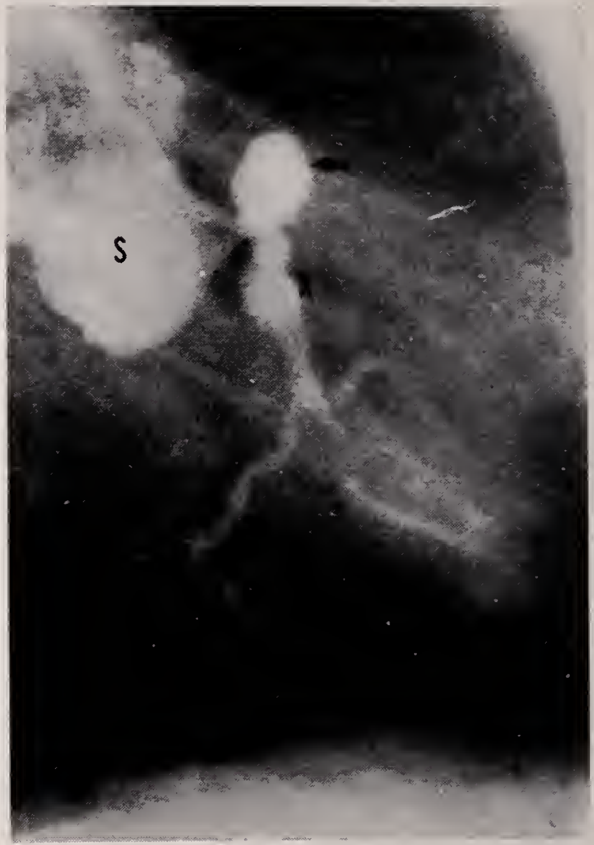

Fig. 4(B)—Case 4; Right coronary-artery injection, shows extensive saccular aneurysmal deformities in the proximal several cms.

On September 14, 1972, an aorto-left anterior descending branch saphenous vein bypass graft under extracorporeal circulation was done. The aneurysmal area felt firm and enlarged. The postoperative course was complicated by anterior myocardial ischemia on EKG which improved with Isordil. There were also chest pains with loss of R-waves in V_2 to V_4. A left lower lobe atelectasis responded to antibiotics and IPPB.

Follow-up on May 22, 1973, revealed that she was feeling much better, having needed only four nitroglycerines in the previous six weeks. Other medications included Dyazide, Aldomet, Isordil and Inderal.

Case 5

A 63-year-old retired farmer had been followed since 1967 when a diagnosis of angina pectoris and hypercholesterolemia was made. By May, 1972, the anginal episodes had become more frequent and intense.

On physical examination, height was 69 inches, weight 176 lbs, b.p. 160/90 and normal pulse. Cardiac examination revealed a mild, diffuse, left ventricular thrust, a grade 2-3 (basis 1-6) systolic, ejection murmur in the third, left interspace and occasional ectopic beats.

Laboratory tests revealed the following: Hb 14.3 gm.%, WBC 4,200, FBS 113 mg.%, cholesterol 309 mg.% and normal triglycerides and urinalysis. Chest Xray showed a prominent heart with a left ventricular configuration. The ECG was abnormal with the T-waves diphasic in I, AVL and V_4 and inverted in V_5 and V_6; there was an occasional ventricular ectopic beat.

On May 10, 1972, a cine-coronary arteriogram was done. The left main coronary artery was unremarkable. Approximately 1 cm. beyond the origin of the left anterior descending branch, there was a mild area of narrowing with a 5-6 mm. saccular aneurysm protruding superiorly (Figure 5). Distal to the aneurysm, there was further 50% narrowing of the AV branch over a distance of 5 mm. with good flow beyond. The left circumflex artery was only moderately well developed and uninvolved except for the origin of the lateral circumflex which was 60-80% narrowed. The right coronary artery was a large, dominant artery until 5-6 cm. beyond the origin which was 60-70% narrowed. Just distal to this, there is a second area of 50% narrowing. The distal one-half of the artery showed diffuse, minimal, atherosclerotic involvement with 50% narrowing just prior to its bifurcation into the posterior descending branch which was moderately well developed. The ventriculogram showed poor contraction of a moderately-severe degree with akinesis of the posterior wall and hypokinesis of the anterior wall. The left ventricular end diastolic pressure was elevated at 10 mm. Hg.

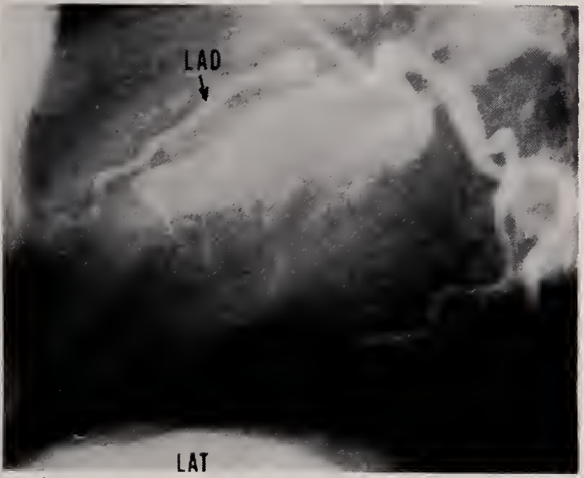

Fig. 5—Case 5; Left coronary-artery injection, lateral view, shows 5-6 mm. saccular aneurysm in the LAD branch.

On June 16, 1972, double saphenous vein bypass grafts were inserted from the aorta to the left anterior descending and right coronary arteries. At operation, an atrial septal defect of the secundum type was found and repaired. The postoperative course was uneventful except for aberrant conduction problems and ventricular ectopics controlled by Quinaglute.

Anginal episodes became less frequent. He was hospitalized briefly in July, 1973, because of congestive heart failure. Discharge medications included Lanoxin, Aldactazide, Isordil and Panwarfin.

Discussion

In the present discussion, to avoid confusion, "aneurysm" defined a more or less demarcated vascular dilatation, "fistula," an abnormal communication between two vascular regions and "shunt," blood flow in a fistula with the direction dependent on pressure gradients. Reviews of coronary-artery aneurysms and fistulas were presented by Packard and Wechsler in 1929 (29 cases)[7], Scott in 1948 (48 cases)[8], Crocker et al., in 1957 (3 cases)[9], Steinberg et al., in 1958 (21 cases)[2], Daoud et al., in 1963 (89 cases) [10] and Kalke and Edwards in 1968 (8 cases)[5].

Scott in 1948[8] reviewed 48 cases and attempted to reclassify all the earlier reported cases. Aneurysms were classified as localized, diffuse or dissecting; also as single, multiple, fusiform or saccular. Localized aneurysms could be single or multiple, congenital or acquired. Diffuse aneurysms were almost always congenital. Acquired causes included atherosclerotic, luetic[11], periarteritis nodosa[12], rheumatic[13], bacterial endocarditis, (mycotic-embolic)[7], traumatic[14] and secondary to neoplasm[15]. Kalke and Edwards in 1968[5] presented the classification outlined in the Table.

TABLE
Classification of Coronary-Artery Aneurysms

- **I. Localized**
  - **1. Congenital**
  - **2. Acquired**
    - **a. Atherosclerosis**
    - **b. Inflammatory**
    - **c. Traumatic**
    - **d. Neoplasm**
    - **e. Arteriovenous fistula**
- **II. Dissecting**
  - **1. Primary**
  - **2. Secondary (to aortic dissecting aneurysm)**
- **III. Diffuse: Arteriovenous fistula**

The most common inflammatory causes are periarteritis nodosa and subacute bacterial endocarditis. Periarteritis nodosa was once considered to be the most common cause of coronary-artery aneurysm. The coronary artery could be solely involved or part of a generalized involvement; these aneurysms could rupture or thrombose. In bacterial endocarditis, all three layers of the arterial wall are involved, resulting in destruction and aneurysm formation. These so-called mycotic-embolic aneurysms more often involved arteries other than the coronary arteries. Dissecting aneurysms of the coronary arteries are usually secondary to a dissecting aneurysm of the ascending aorta. Hirst et al. in 1958[16] reported that in 505 cases of aortic dissecting aneurysm, extension occurred into the coronary arteries in 39 cases (8%). Rarely, dissection begins in the coronary arteries, the so-called primary dissection. Brody et al. in 1965[17] reviewed 14 such cases (four their own) and felt that the pathogenesis was either cystic medial necrosis or a primary hemorrhage into the media. Twelve of their 18 patients were female and six of the aneurysms were recognized shortly after pregnancy. Brody suggested that anoxia may augment the formation of dissecting aneurysms.

Congenital aneurysms with or without fistulas more commonly involve the right coronary artery whereas acquired aneurysms are predominantly left-sided[8,18]. The age range is 14 months to 87 years. The male: female ratio is 14:1[19]. The aneurysm may be asymptomatic or there can be chest pains and symptoms of congestive failure. On auscultation, the most common finding when a fistula is present is a precordial, usually continuous, murmur. The embryology of coronary-artery malformations is presumed to be caused by one of three mechanisms[19]. When a coronary-artery communicates with a cardiac chamber (usually right side), vein, coronary sinus or pulmonary arterial trunk, an arteriovenous fistula develops. The shunt that occurs through the anomalous channel often causes a diffuse dilation and tortuosity of the involved coronary artery, a so-called diffuse aneurysm. In some such cases one or more saccular aneurysms (some with calcific walls) may occur in the dilated vessels. These saccular aneurysms are acquired complications of abnormally dilated arteries taking part in an arteriovenous fistula. Another congenital malformation in the coronary arteries is the isolated saccular aneurysm in the absence of an arteriovenous fistula. This probably results from a congenital deficiency of the media and elastic layers at the bifurcation of vessels as Forbus in 1930[20] suggested as being responsible for cerebral berry aneurysms. Bishop et al. in 1974[21] reviewed the fact that myocardial ischemia has been noted in 7% of patients with coronary-artery fistulas; six patients have been described with previous myocardial infarctions and they added one case of their own.

Daoud et al. in 1963[10] reviewed 89 cases (10 of their own) of coronary-artery aneurysms, all diagnosed at post-mortem. Sixty-seven were in males, a male:female ratio of 3:1. Etiologically, 48 (52%) were due to atherosclerosis, 11% mycotic-embolic, 11% dissecting, 4% luetic and five cases indeterminate. Of the 48 cases of atherosclerotic coronary-artery aneurysms, 38 were in males usually between 50-70 years of age. In 12 of the 48 cases, the aneurysms were multiple. In 16 cases was the terminal episode attributed to a catastrophic event directly related to the presence of the aneurysm. Of their 10 personal cases, all were atherosclerotic in type with the coronary arteries and in most cases the aorta showing advanced atherosclerosis. Three of the 10 cases had multiple aneurysms. Seven aneurysms were located in the right coronary artery, two in the left coronary artery and one in both vessels. Surprisingly, in eight of the 10 cases, death was directly related to an associated abdominal aortic aneurysm (either rupture or a complication of repair).

Kalke and Edwards in 1968[5] reported on eight cases of localized coronary-artery aneurysms studied pathologically. The aneurysm was responsible for death in four cases and only one aneurysm was recognized during life by coronary arteriography. Of the eight aneurysms, six were due to atherosclerosis, one to periarteritis nodosa and one congenital. The six atherosclerotic aneurysms were predominantly in males over 45 years of age and were associated with extensive atherosclerosis in the coronary-artery system. There was massive deposition of lipoid material in the intima and the underlying media was focally destroyed leading to aneurysm formation. In three of the six cases, the cause of death was directly related to the aneurysm. Of the six aneurysms, four were localized (three in the right coronary and one in the left coronary artery). In two cases, the aneurysms were multiple (in one case there were two aneurysms in the right and one in the left anterior descending). The right coronary artery was more commonly involved by localized coronary-artery aneurysms than the left coronary artery.

The pathogenesis of atherosclerotic coronary-artery aneurysms involves several factors. Atherosclerosis causes the deposition of lipoid material in the intima and the focal destruction of the media, thus weakening the arterial wall. Holman[22] postulated that a proximal zone of stenosis with dilation beyond initiated the process of aneurysm formation. When the blood stream is ejected through the stenotic area under high velocity, it strikes a slower moving blood current. The clash of the two streams (fast and slow) produces alternating high and low pressures, turbulence and high kinetic energy converting to lateral pressure and inducing structural fatigue on the elastic wall. The complications of such aneurysms are rupture[7], myocardial ischemia and infarction[21] and rarely endocarditis[23]. The finding of such an aneurysm during life by arteriography may allow certain cases to be treated surgically.

Summary

Five cases of atherosclerotic aneurysms of the coronary arteries are presented. All were diagnosed by cine-coronary arteriography during life and occurred in 1.8% of such arteriograms performed over a two-year period. None were examined pathologically. Surprisingly, four cases were in females with an average age of 50 years (range 32 to 62 years). All five cases had hypercholesterolemia and severe two to three vessel coronary-artery disease. Three cases eventually came to saphenous-vein bypass graft surgery. Three cases had previous myocardial infarctions. One had associated rheumatic heart disease and another an atrial septal defect. One of the five cases had two aneurysms. Four aneurysms were located in the left anterior descending branch, one in the circumflex artery and one in the right coronary artery.

Coronary-artery aneurysms are probably not as rare as the previous low number of case reports. Cine-coronary arteriography will allow more to be recognized during life and surgically corrected.

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Thrombophlebitis—Pierach et al. (Page 165)

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Thrombophlebitis

Some Practical Aspects

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Thrombophlebitis may be superficial and harmless or deep and potentially life threatening. It can be prevented to a great extent, and this prophylaxis with physio-therapeutic measures and anticoagulants is more effective and gratifying than its treatment.

THROMBOPHLEBITIS, if limited to a superficial vein, can be a relatively harmless disease, if properly managed. But if it persists, recurs or involves deeper veins, it can develop into a chronic, all too often life-threatening problem. The following recommendations are offered to help in the handling of various forms of thrombophlebitis.

The localization of a thrombophlebitis, whether it is superficial or deep, determines treatment and influences the prognosis. Here, venography, a relatively harmless procedure, is extremely helpful, not only in delineating the site and extent of venous obstruction, but also in assessing eventual collateral circulation.[1]

Acute superficial phlebitis can easily be diagnosed by feeling a tender, inflamed cord-like subcutaneous vein. In the arms, this is often preceded by intravenous injections, especially by prolonged infusions. In the legs, varicose veins predispose to the occurrence of superficial thrombophlebitis. Systemic signs, aside from low grade fever, are usually absent, and except for some localized swelling, there is no peripheral edema. Superficial thrombophlebitis of the chest wall (Mondor's disease) is harmless.[2]

Treatment of superficial thrombophlebitis can be accomplished by bed rest, usually for a week. Salicylates and warm, moist pads help in managing inflammation and the accompanying pain. If the disease spreads, for example, from below to above the knee, elevation of the extremity and anticoagulants are indicated. The prognosis is good. Should the problem persist or recur, one should think of an underlying malignancy, especially of the pancreas.[3] If varicose veins are a contributing cause, high ligation and stripping may be indicated.

Deep thrombophlebitis is not only more serious, but often difficult to diagnose. It can be unrecognized and present itself with pulmonary embolism as the first sign. If a patient complains of pain, swelling, or tenderness in one calf after an operation, after childbirth, or during prolonged bed rest, a deep calf thrombophlebitis should strongly be considered. As there are many collateral venous channels, generalized edema occurs late. Homan's sign (calf pain during acute dorsiflection of the foot) is, if present, a good indicator of deep thrombophlebitis, but is absent in more than half of proven cases of calf vein thrombophlebitis. Newer techniques like scanning with radioactively-tagged fibrinogen are helpful but not yet widely available.[4]

The treatment consists of bed rest in Trendelenburg position (elevation of the foot of the bed to about 20°, with the body held straight, carefully avoiding pooling of blood in the pelvic area), and anticoagulation. As oral anticoagulants take two to three days before they achieve their therapeutic goal, heparin should be started initially. A six-week program on anticoagulants is often indicated.[5]

Opinions about the best way of administering and monitoring heparin therapy vary. We use to good advantage the following schedule: 5,000 U heparin i.v. every four hours. The whole blood clotting time should be at twice the control value for several hours after each injection. The activated partial thromboplastin time (APTT) may also be used as a guide in heparin therapy.[6] It should be between 60 and 100 sec (with a normal control around 35 sec). But one might also elect not to monitor heparin therapy with any laboratory tests and adhere instead to the above mentioned standard doses, where the major advantage is simplicity.

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Oral anticoagulants such as warfarin sodium (Coumadin®) should be started at the same time with an initial dose between 20 and 40 mg and half of this dose on the second and third days. The prothrombin time serves as a guide, the therapeutic range being two and a half times the control. This level is usually reached after three days. Heparin therapy should continue for another three to four days. Fatal embolism can occur in spite of adequate anticoagulation, although the incidence is not known.

Thrombophlebitis during pregnancy deserves special attention. The above mentioned Trendelenburg position can and should be maintained even up to delivery without too much discomfort. Oral anticoagulants are contraindicated as they pass through the placenta (as well as into the milk of nursing mothers) and risk the fetus' life, but heparin can be injected, as it does not cross the placental barrier.

A special form of deep thrombophlebitis is the involvement of a major venous trunk, *phlegmasia cerulea dolens*. Here the extremity is swollen, tender, and cyanotic with a reddish tinge. In the leg this can occur from extension of a deep calf thrombophlebitis, but also postpartum, posttraumatic, or postoperatively. If it involves the vena cava, both legs are swollen, and cyanotic. On the upper extremities phlegmasia cerulea dolens can be preceded by vigorous use of the arms, but it may also be the first hint for mediastinal malignancy. It should be treated like a deep thrombophlebitis, but thrombectomy, fasciotomy and dextran infusion are alternative or additional therapeutic modalities.[7]

The *prophylaxis of thrombophlebitis*. As most of the pulmonary emboli originate from the lower extremities and to some extent from the pelvis, preventive measures have been directed mostly to these areas. Elastic stockings, elevation of the foot of the bed, leg exercises, and early ambulation offer some prophylaxis.[8] More elaborate physical techniques like electrical stimulation of calf muscles or active rhythmic compression by pneumatic devices show some promise but are still experimental.

Oral anticoagulation can be employed even during surgery, if the prothrombin time is below the double normal control.[9] Particular attention should be given to other drugs that might influence the effect of anticoagulants.[10] Small subcutaneous doses of heparin have also been shown to decrease markedly the incidence of deep venous thrombosis.[11] Here, 5000 U heparin are given two hours before and every eight to twelve hours after operation. All anticoagulation can be discontinued once the patient is fully ambulatory. The use of other "anticoagulants" such as aspirin, dextran, dipyridamole and sulfinpyrazone has so far not yet shown its superiority over the classical drugs, warfarin and heparin.

Surgical Intervention in Thromboembolism

Vena cava clip. Clipping or plication of the vena cava is indicated, when pulmonary emboli recur in spite of adequate anticoagulation. If anticoagulants are contraindicated or if septic pulmonary emboli occur, surgical interruption of the inferior vena cava may be considered. The transcutaneous insertion of an umbrella like filter[12] into the inferior vena cava is attractive especially in the very ill or obese patient.

Pulmonary embolectomy, a heroic measure, is *only* indicated in the face of persistent hypotension and when angiography shows at least 60% of the pulmonary arterial bed to be occluded.[13] The use of fibrinolytic agents such as streptokinase and urokinase found wide acceptance in Europe, and a careful cooperative study showed that urokinase is a good alternative in the treatment of massive pulmonary embolism.[14]

In the final analysis, however, it is all too clear, that prophylaxis is by far the better approach and superior to all forms of treating pulmonary embolism.

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4-14. Will be found on page 163.

Intravenous Hydrochloric Acid in the Treatment of Metabolic Alkalosis

Use in Acute Renal Failure

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A patient with acute renal failure and metabolic alkalosis was treated with intravenous hydrochloric acid (with and without peritoneal dialysis). A 0.15 normal solution of hydrochloric acid was used, and the maximum rate of administration was 325 mEq/day. Seventeen previous case reports of intravenous hydrochloric used to treat metabolic alkalosis are reviewed. The major indication for the use of this therapy in metabolic alkalosis is acute renal failure. A second indication may be hepatic failure.

THE MANAGEMENT OF metabolic alkalosis accompanied by renal failure presents a difficult problem for the clinician. The presence of renal failure severely limits the use of the standard treatment modalities in metabolic alkalosis: volume replacement, saline and potassium chloride.[1-4] Eichenholz et al.[5] discussed the successful use of potassium chloride in azotemic patients with metabolic alkalosis, but none of their patients exhibited acute oliguric renal failure. Isolated reports of the use of intravenous hydrochloric acid in this difficult clinical situation have appeared in the literature.[6-12] The case report which follows illustrates the successful use of hydrochloric acid in the management of metabolic alkalosis complicated by oliguric renal failure.

Methods and Materials

Laboratory tests were performed by standard techniques. The 0.15N hydrochloric acid (HCl) solution for intravenous infusion was prepared by adding 12.5 ml of reagent grade (35%) HCl (Mallinckrodt) to 1000 ml of sterile distilled water for injection. Chloride assay was performed on all bottles of HCl (method of Schales and Schales)[13] and varied between 140-146 mEq/liter.

Case Report

The patient was a 34-year-old man, known alcoholic, who entered Minneapolis Veterans Administration Hospital with a two-week history of vomiting and abdominal pain. He had been hospitalized at another hospital for the week before transfer to the Veterans' hospital. The transfer summary mentioned that the patient had vomited continuously around his nasogastric tube, had shown signs of delirium tremens and was thought to be dehydrated.

The patient was an obtunded adult man with warm, dry skin. The pulse was 120/min, the blood pressure 130/76 mm Hg, the temperature 39.5°C rectally, and the central venous pressure 15 cm H_2O. The sclerae were icteric, and his tongue was dry. The lungs and heart were normal. His abdomen was slightly distended, and there were no scars. There was moderate tenderness to deep palpation in the mid-epigastrium and a vague suggestion of an epigastric mass. Bowel sounds were absent, and an abdominal succussion splash was present. Rectal examination was normal except that the stool tested positive for occult blood. A nasogastric tube was passed on admission, and 1500 ml of fluid containing occult blood was aspirated. Catheterization of the urinary bladder yielded only 50 ml of urine.

On admission the hemoglobin was 10.2 gm/100 ml, the hematocrit 31.5 vol %, and the white blood cell count 14,500/mm^3. The urine specific gravity was 1.015. The urine pH was 7 and contained 2+ protein, 4-5 red blood cells and 8-10 white blood cells per high power field, the sodium, 138 mEq/l; the potassium, 4.3 mEq/l; the chloride, 66 mEq/l; the CO_2 combining power, 53.2 mM/l; the calcium, 6 mg/100 ml; the phosphate, 9.7 mg/100 ml; the glucose, 163 mg/100 ml; the BUN, 114 mg/100 ml; the serum glutamic oxaloacetic acid (SGOT), 250 Kormen units (normal 10-40); the serum lactic dehydrogenase (LDH), 350 Wacker units (normal 30-120); the total bilirubin, 5.0 mg/100 ml; the serum amylase, 195 units/100 ml (normal 300); the albumin,

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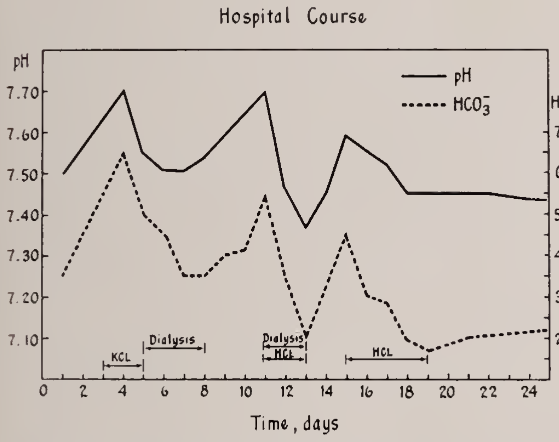
2.6 Gm/100 ml; the urine sodium, 25 mEq/1; the urine potassium, 89 mEq/1 and the urine amylase, 195 units (normal 300). Arterial blood gas values were pH, 7.63; pCO_2, 49.5 mm Hg; HCO^-_3, 50.8 mM/1, and pO_2, 54 mm Hg. Cultures of blood and urine were sterile. Sputum cultures grew non-pathogenic organisms. Liver biopsy, early in the hospital course, showed fatty metamorphosis, periportal inflammation, and mild bile stasis. Initial impressions were: (1) gastric outlet obstruction of undetermined etiology, (2) upper gastrointestinal bleeding of unknown etiology, (3) metabolic alkalosis, secondary to number 1, (4) alcoholic liver disease, and (5) acute azotemia, with oliguria of unknown etiology.

Hospital Course (Figure)

Initially, the alkalosis was treated with parenteral potassium chloride, a total of 500 mEq over 48 hours. Anuria and hyperkalemia (potassium, 7.0 mEq/l) prevented the further administration of KCl. At this point, with the BUN 146 mg/100 ml and creatinine 16.5 mg/100 ml, peritoneal dialysis was begun and continued over 72 hours (a total of 71 two liter exchanges with 1.5% Impersol (Abbott) with 5 mEq/l of potassium chloride).



Figure—Graphic illustration of the patient's acid-base status. Illustrated are the variations in arterial blood pH and bicarbonate concentrations in response to treatment.

At the conclusion of the first course of peritoneal dialysis (day number eight) blood chemistries were as follows: sodium, 142 mEq/l, potassium, 6.4 mEq/l; chloride, 84 mEq/1; CO_2 combining power, 41 mM/1; and BUN, 55 mg/100 ml. The arterial blood pH was 7.53; pCO_2, 50 mm Hg; HCO_3, 40.7 mM/1, and the pO_2 was 47 mm Hg. The gastric outlet obstruction persisted with nasogastric returns averaging 2 liters/24 hours, and oliguria continued (urine volume averaged 150 ml/24 hours).

On day 11, the patient's arterial blood pH was 7.70; bicarbonate, 60 mM/1; pCO_2, 55 mm Hg; serum chloride, 61 mEq/1; and serum potassium, 5.8 mEq/1. An infusion of 0.15 normal HCl (see methods section) was begun into a central venous catheter. A total of 265 mEq of HCl were given over 40 hours. Because of a marked weight gain, indicating overhydration, another peritoneal dialysis was begun during the HCl infusion.

For this second course of peritoneal dialysis, a solution of 5% dextrose in 0.9% NaCl with 1.5 mEq/l of magnesium, 3.5 mEq/1 of calcium and 3 mEq/l of potassium added was used as the dialysate. Thus, lactate was excluded in an attempt to facilitate correction of the plasma bicarbonate level. At the conclusion of approximately 48 hours of 50 minute exchanges and continued HCl infusion as outlined above, the arterial blood pH was 7.35; the pCO_2, 47 mm Hg; the HCO^-_3, 24.8 mM/1; and the pO_2, 81 mm Hg.

Two days later, the continuing gastric outlet obstruction, severe metabolic alkalosis recurred for a third time, with the pH rising to 7.60 and bicarbonate to 50 mM/1. This time the nasogastric aspirate was replaced volume for volume with a 0.15 N solution of HCl prepared in a manner similar to that described above. On this occasion, 325 mEq/day of HCl were given over four days. Peritoneal dialysis was not instituted. The arterial blood pH fell to 7.45 and remained normal. Subsequently, the renal failure relented, and the patient was transferred to surgery. Earlier, repeated endoscopy and upper gastrointestinal radiography failed to reveal a lesion explaining either the continued bleeding or the outlet obstruction. At laparotomy, the findings were those of acute pancreatitis and peripancreatic inflammation. The patient was eventually discharged in acid-base balance without evidence of pancreatic or renal disease.

Discussion

The standard therapy for metabolic alkalosis includes replacement of fluid volume, sodium chloride, and potassium. The role of the potassium ion in the pathogenesis of metabolic alkalosis is controversial;[3] nonetheless potassium deficiency usually coexists with the alkalosis. Therefore, replacement of potassium deficits in the form of potassium chloride is customary. The combination of acute renal failure and severe metabolic alkalosis is unusual. The presence of oliguria limits the amounts of sodium, potassium and volume that can be tolerated. Eichenholz et al.[5] have discussed the problem of metabolic alkalosis associated with azotemia and have suggested that the latter does not contraindicate the use of potassium chloride. The patients they reported, however, were not oliguric and may have had prerenal azotemia on the basis of dehydration. Our patient had acute azotemia with oliguria and was not dehydrated. Consequently, treatment of the alkalosis with large volumes of sodium chloride was contraindicated. Potassium chloride was given until hyperkalemia with cardiac arrhythmia supervened.

Ammonium chloride has been suggested as an adjunct to the standard therapy[14] of metabolic alkalosis in difficult cases. Ammonia has been implicated in the pathogenesis of hepatic encephalopathy in patients with liver disease.[15] Our patient had evidence of hepatic dysfunction, and, therefore, we felt that ammonium chloride was contraindicated. Two other agents infrequently used in the treatment of metabolic alkalosis, L-lysine monohydrochloride and arginine hydrochloride, were not used in this case.

In contrast to metabolic acidosis, metabolic alkalosis by itself is not generally considered to be life threatening. It is well recognized that it can result in tetany and convulsions.[16] Although significant respiratory compensation is unusual, it can result in hypoventilation and hypoxemia.[10,17] The latter complication was exhibited by our patient.

Seventeen case reports of patients with metabolic alkalosis treated with IV hydrochloric acid have appeared in the medical literature.[6-12] The concentration of the hydrochloric acid solutions used varied from 0.05 N to 0.20 N. The total amount administered ranged from 50 mEq to 765 mEq. The maximum rate of administration was 600 mEq/24 hours.[12] Several authors mention that the mode of administration was via central venous pressure catheter.[8,12] None of the authors reported complications directly related to the hydrochloric acid, and fourteen of the seventeen patients survived. Fatalities were related to acute renal failure, pancreatitis, and respiratory failure,[6] bilateral salpingitis with peritonitis and massive intracerebral hemorrhage.[11] At autopsy, in one of these cases,[7] the superior vena cava (site of administration of the hydrochloric acid) was inspected and no intimal damage was noted. Frick and Senning[7] performed *in vitro* studies adding hydrochloric acid to washed red blood cells, plasma, and whole blood. There was no evidence of hemolysis or plasma protein precipitation at concentrations reached in the therapeutic situation. Abouna, et al.[12] reported eight patients treated with intravenous HCl. They noted no change in the patients' hematocrits after the administration of the HCl.

The patient reported here received intravenous hydrochloric acid on two occasions. On the first occasion, he received a total of 265 mEq of HCl accompanied by peritoneal dialysis. On the second occasion, a total of 1300 mEq administered over four days was effective without dialysis. During the second period of hydrochloric acid administration, the patient's hemoglobin did drop from 11.7 gm/100 ml (on day thirteen) to 8.3 gm/100 ml (on day eighteen). There are several possible explanations for this phenomenon: (1) dilution (the serum sodium concentration fell and the body weight increased), (2) gastrointestinal bleeding (noted before, during and after the hydrochloric acid therapy), (3) uremia, and (4) the fall in hemoglobin might have represented hemolysis secondary to the hydrochloric acid, but this was not evaluated in this case. However, as mentioned above, Frick and Senning[7] demonstrated *in vitro* that hemolysis does not occur with hydrochloric acid in therapeutic concentrations. It appears there were no complications or toxic effects from the hydrochloric acid although the possibility of hemolysis was not rigorously excluded.

The major indication for the use of hydrochloric acid is in treating metabolic alkalosis accompanied by severe acute renal failure. A second indication may be hepatic failure. Also, administration of intravenous hydrochloric acid should be via central venous catheter.

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Gonorrhea Screening in Olmsted County during 1974

G. R. PETTERSEN, M.D.[*] and LYLE A. WEED, M.D.[†]

A total of 7,416 specimens were submitted for gonorrhea screening from six different sites around Rochester. Forty-two cases of gonorrhea were discovered for an incidence of 0.57%.

DURING A 12-MONTH period in 1974, 7,416 women participated in a screening program for gonorrhea. This program was financed by funds that the Minnesota Department of Health received from the federal government for venereal disease control. It is common knowledge that women can be asymptomatic carriers of gonorrhea. If one could detect these carriers through some screening procedure and provide treatment for them, then supposedly the incidence of gonorrhea would be decreased in the community. The objective was to provide this screening procedure to the largest number of women possible.

Preliminary Planning

The Olmsted County Health Department established a bacteriological laboratory under the direction of Dr. Weed. The equipment and supplies were obtained from the State Health Department. The specimens were processed in conformance with the information obtained in the manual "Criteria and Technique for the Lab Diagnosis of Gonorrhea."

Contact was established with Rochester Planned Parenthood and the Olmsted Medical and Surgical Group and they agreed to cooperate with this screening procedure. In February the Rochester State Hospital was included. March saw St. Mary's Hospital Health Service and the Olmsted Community Hospital brought into the program. In June the Preventive Medicine Division at Mayo Clinic began sending specimens.

Methodology

Every woman between the ages of 15 and 45 having a pelvic examination would also have cervical and urethral cultures taken which were streaked directly onto Thayer-Martin medium. These plates were kept in candle jars until they were transported to the health department.

In the health department's laboratory the plates were identified and the information entered in a log book. They were then incubated in candle jars at 35°C. The plates were examined at 24, 48, and 72 hours. Slides were made of oxidase positive colonies and carbohydrate fermentation tests were done for identification of N. gonorrhoeae. Reports were sent daily with the pickup courier to the screening sites.

Results

The Table gives the total tests done plus the number of positives discovered from each testing site. A total of 7,416 specimens was collected from the seven testing sites. The Olmsted Medical and Surgical Group provided 4,308 of these specimens while at the other extreme the Olmsted Community Hospital provided only 24. Altogether 42 cases of gonorrhea were discovered which gives an incidence of 0.57%. The greatest number of positives was 24 provided by the Olmsted Medical and Surgical Group which also had 58% of the total specimens tested.

Discussion

The total expense for the gonorrhea screening was:

TABLE

	Planned Parent.	Olmsted Medical Surgical Group	Rochester State Hospital	St. Marys Health Center	Olmsted Commty. Hosp.	Mayo Clinic	Totals
Number Screened	2,322	4,308	51	274	24	437	7,416
Positive for Gonorrhea	10	24	1	3	3	1	42
Percent Positive	0.43%	0.56%	2.0%	1.1%	12.5%	0.23%	0.57%

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[*] Director of Public Health, Olmsted County Health Department, Rochester, Minnesota.

[†] Deputy Director of Public Health, Olmsted County Health Department; Emeritus Staff, Mayo Clinic, Rochester, Minnesota.

Part-time medical laboratory assistant	$4,715
Mileage expense (courier service)	1,487
Miscellaneous expense	25
Total	$6,227*

Using this sum ($6,227) one calculates a unit cost of 84¢ per patient tested. By these computations it costs $148.26 to detect one case of gonorrhea. It becomes obvious that the incidence of gonorrhea in the unsuspecting population of Olmsted County is at a level that makes it costly to find one case by this screening procedure. Gonorrhea is a disease that can be present in spite of the fact it may be asymptomatic in both males and females, but in order to detect these asymptomatic cases a great deal of time and effort is necessary.

By way of contrast the Venereal Disease Clinic at the Olmsted County Public Health Center attracts both males and females who suspect they may have venereal disease or at least have some concern about urogenital difficulties. During the same 12 month period of time, 781 patients were seen at the Health Center, and 100 cases of gonorrhea were diagnosed for an incidence of 12.8%.

The Minnesota Department of Health received reports for 225 cases of gonorrhea in Olmsted County in 1974, compared with 125 cases in 1973 (an 80% increase). Undoubtedly, the screening program uncovered some cases which would not have otherwise been found. One must also assign a certain proportion of the increase to better reporting due to enhanced physician awareness.

Conclusion

From an economic standpoint it is expensive to screen the general population of Olmsted County to detect gonorrhea. Selective screening may yield better results, but certainly the population participating in sexual intercourse with more than one partner needs to be aware of the possibilities of acquiring gonorrhea, needs to assume the responsibility for detection of the disease and needs medical facilities readily available where they can be examined, treated and counseled promptly and confidentially.

Summary

The screening sites participating in this year-long program for gonorrhea gave excellent cooperation in this study. In spite of an 80% increase in reported gonorrhea in the community, the expense involved with this screening procedure encourages one to look for alternatives.

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*This cost does not include the Thayer-Martin plates which were furnished by the Minnesota Department of Health.

Minnesota Society of Clinical Pathologists

Symposium of Salivary Glands and Pancreas
Saturday, April 10, 1976
Health Sciences Building, University of Minnesota

9:45-10:00 a.m.	Welcome Address and Announcements, Dr. Charles Chedister, M.D.
10:00-11:00 a.m.	Pathology of the Pancreas, Roy G. Shorter, M.D.
11:00-11:30 a.m.	Pancreatic Function Testing, Desmond Burke, M.D.
11:30-12:00 a.m.	Diagnosis of Acute Pancreatitis, Eugene P. DiMagno, M.D.
12:00- 1:30 p.m.	Luncheon at Campus Club, Coffman Union
1:30- 2:00 p.m.	Cystic Fibrosis, Warren Warwick, M.D.
2:00- 2:30 p.m.	Functioning Islet Cell Tumors, Laboratory Aspects, Edward Wong, M.D.
2:30- 3:00 p.m.	Sjogren's Syndrome Laboratory Aspects, Gene G. Hunder, M.D.
3:15- 4:15 p.m.	Tumors of Salivary Glands Benign Tumors, Juan Rosai, M.D. Malignant Tumors, Louis P. Dehner, M.D. Tumor-Like Conditions, Bruce F. Hertel, M.D.

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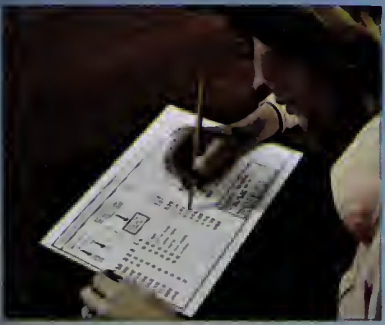
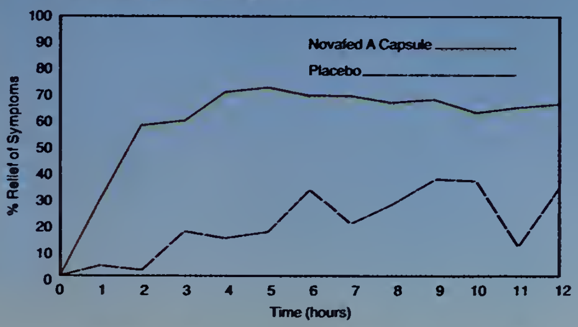
Prompt onset of effect is followed by full 12-hour relief.

(Please refer to the following page for bioavailability studies and prescribing information.)



Patients with severe pollen allergies were tested during hay fever season in a countryside environment and asked to rate severity of five different symptoms on a scale of 1 to 4.

Clinical Study: Degree of Relief from Itchy Eyes and Nose and Throat, Watery Eyes, Runny Nose*



*Unpublished data, Medical Department Files, Dow Pharmaceuticals, The Dow Chemical Company, Indianapolis, Indiana.

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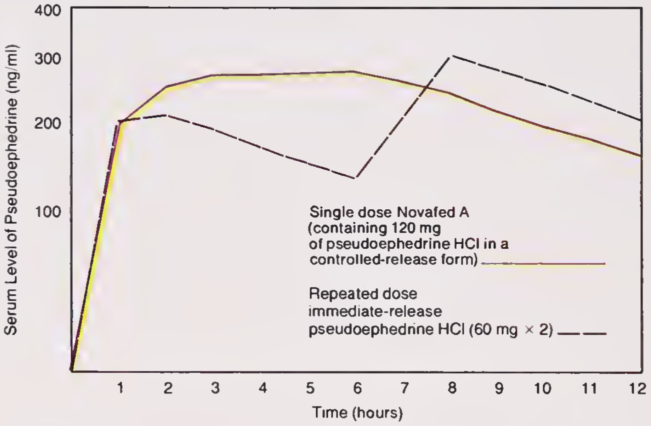
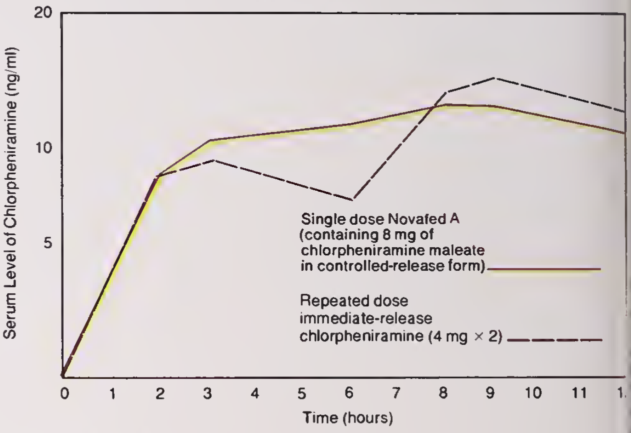
The chart at the left shows the serum levels of pseudoephedrine. Initial serum levels following one Novafed A Capsule were comparable to those following a single dose of 60 mg. pseudoephedrine hydrochloride in an immediate-release form. Serum levels of pseudoephedrine over a 12-hour period following a single dose of Novafed A were also comparable to those obtained by an immediate-release form taken every 6 hours.

The chart at the right shows the serum levels of chlorpheniramine. Initial serum levels following one Novafed A Capsule were comparable to those followin a single dose of 4 mg. chlorpheniramine maleate in an immediate-release form. Serum levels of chlorpheniramine over a 12-hour period following a single dose of Novafed A were also comparable to those obtained by an immediate-release form taken every 6 hours.

Comparison of Mean Serum Levels of Pseudoephedrine Following Novafed A and an Immediate-Release Reference Formulation*



Comparison of Mean Serum Levels of Chlorpheniramine Following Novafed A and an Immediate-Release Reference Formulation*



*Unpublished data, Medical Department Files, Dow Pharmaceuticals, The Dow Chemical Company, Indianapolis, Indiana.

DESCRIPTION: Each NOVAFED A capsule contains 120 mg. of pseudoephedrine hydrochloride and 8 mg. of chlorpheniramine maleate. The specially formulated pellets in each capsule are designed to provide continuous therapeutic effect for about 12 hours. Nearly one-half of the active ingredients is released soon after administration and the remainder is released slowly over the remaining time period.

ACTIONS: NOVAFED A combines the action of a nasal decongestant, pseudoephedrine hydrochloride, and an antihistamine, chlorpheniramine maleate. These ingredients are combined to provide prompt and sustained nasal and upper respiratory decongestant and antihistaminic action.

INDICATIONS: NOVAFED A is indicated for the relief of nasal congestion and eustachian tube congestion associated with the common cold, sinusitis and acute upper respiratory infections. It is also indicated for perennial and seasonal allergic rhinitis, vasomotor rhinitis, allergic conjunctivitis due to inhalant allergens and foods and for mild, uncomplicated allergic skin manifestations of urticaria and angioedema. Decongestants in combination with antihistamines have been used for many years to relieve eustachian tube congestion associated with acute eustachian salpingitis, aerotitis media, acute otitis media and serous otitis media. NOVAFED A may be given concurrently, when indicated, with analgesics and antibiotics.

CONTRAINDICATIONS: Symphathomimetic amines are contraindicated in patients with severe hypertension, severe coronary artery disease, and in patients on MAO inhibitor therapy. Antihistamines are contraindicated in patients with narrow-angle glaucoma, urinary retention, peptic ulcer, during an asthmatic attack, and in patients receiving MAO inhibitors.

Children under 12: NOVAFED A controlled-release capsules should not be used in children less than 12 years of age.

Nursing Mothers: Pseudoephedrine is contraindicated in nursing mothers because of the higher than usual risk for infants from sympathomimetic amines.

Hypersensitivity: This drug is contraindicated in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines or antihistamines. Patient idiosyncrasy to adrenergic agents may be manifested by insomnia, dizziness, weakness, tremor or arrhythmias.

WARNINGS: Sympathomimetic amines should be used judiciously and sparingly in patients with hypertension, diabetes mellitus, ischemic heart disease, increased intraocular pressure, hyperthyroidism, or prostatic hypertrophy. Sympathomimetics may produce central nervous system stimulation and convulsions or cardiovascular collapse with accompanying hypotension.

Antihistamines may impair mental and physical abilities required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery, and mental alertness in children. Chlorpheniramine maleate has an atropine-like action and should be used with caution in patients with increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension or in patients with a history of bronchial asthma.

Do not exceed recommended dosage.

Use In Pregnancy: The safety of pseudoephedrine for use during pregnancy has not been established.

Use In Elderly: The elderly (60 years and older) are more likely to have adverse reaction to sympathomimetics. Overdosage of sympathomimetics in this age group may cause hallucinations, convulsions, CNS depression, and death. Therefore, safe use of a short-acting sympathomimetic should be demonstrated in the individual elderly patient before considering the use of a sustained-action formulation.

PRECAUTIONS: This drug should be used with caution in patients with diabetes, hypertension, cardiovascular disease and hyperreactivity to ephedrine. The antihistaminic may cause drowsiness and ambulatory patients who operate machinery or motor vehicles should be cautioned accordingly.

ADVERSE REACTIONS: Hyperreactive individuals may display ephedrine-like reactions such as tachycardia, palpita tions, headache, dizziness, or nausea. Patients sensitive to antihistamines may experience mild sedation.

Sympathomimetic drugs have been associated with certai untoward reactions including fear, anxiety, tenseness, restlessness, tremor, weakness, pallor, respiratory difficulty, dysuria, insomnia, hallucinations, convulsions, CN depression, arrhythmias, and cardiovascular collapse wit hypotension.

Possible side effects of antihistamines are drowsiness, restlessness, dizziness, weakness, dry mouth, anorexia, nausea, headache and nervousness, blurring of vision, heartburn, dysuria and very rarely, dermatitis.

DRUG INTERACTIONS: MAO inhibitors and beta adrenergi blockers increase the effect of sympathomimetics. Sympathomimetics may reduce the antihypertensive effects o methyldopa, mecamylamine, reserpine and veratrum alkaloids. Concomitant use of antihistamines with alcoho tricyclic antidepressants, barbiturates and other central nervous system depressants may have an additive effect.

DOSAGE AND ADMINISTRATION: One capsule every 12 hours. Do not give to children under 12 years of age.

CAUTION: Federal law prohibits dispensing without prescription.

HOW SUPPLIED: NOVAFED A is supplied in red and oran colored hard gelatin capsules, monogrammed with the Dow diamond followed by the number 109, in bottles of 100.

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Editorials

Transverse Myelopathy in Heroin Addiction

NEUROLOGIC SYNDROMES are increasingly recognized as significant consequences of self-administered intravenous narcotics, especially in heroin addicts. Among the most devastating noninfectious neurologic complications is the transverse myelopathy syndrome. The nicely documented case reported by Lee, Randa, and Gold* affords an improved understanding of the pathogenesis of this condition.[1] The site of the lesion and the involvement of the anterolateral spinal cord structures strongly supports their conclusion of ischemic etiology. It is problematic at this time whether the hypotension and hypoxia presumed to be the mechanism of the ischemia are related to the heroin itself or to the diluents and contaminants used to cut the drug. Quinine, which is a common diluent, when injected intravenously may cause severe hypotension and acute circulatory failure. The possibility of allergic or hypersensitivity reaction is mentioned in other communications.[2] Hyperimmunoglobulinemia is reported in heroin addiction and may be related to antigenicity of diluents and contaminants.[3]

It is not entirely clear why hypotension and hypoxia would result in spinal cord infarction without significant evidence of cerebral ischemia. Silver and Buxton have demonstrated that this situation can occur in cardiac arrest and in other causes of severe hypotension and circulatory failure.[4]. It is possible that the bizarre postures sustained for long periods which may be seen in heroin intoxication may contribute to the development of spinal cord ischemia without cerebral ischemia. Lee, Randa and Gold have made a significant contribution with their convincing demonstration of spinal cord infarction as the probable cause of the transverse myelopathy syndrome in heroin addiction.

John M. McKelvey, M.D.
Minneapolis, Minnesota

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*Minnesota Medicine 59:2:82, 1976.

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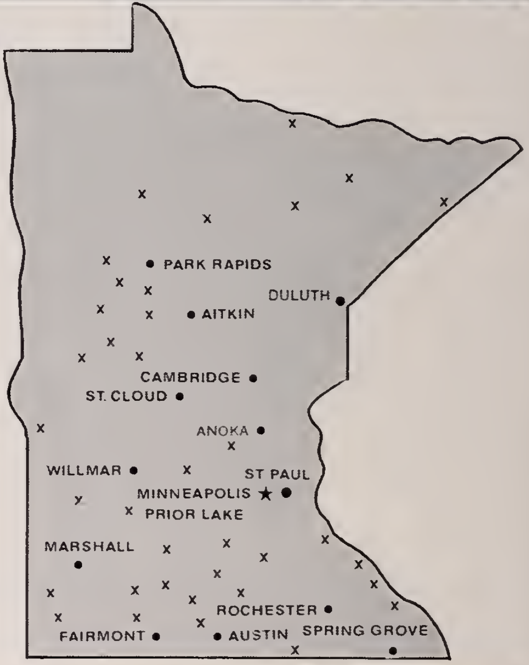

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Two Primary Intracranial Tumors

The article titled, "Two Primary Intracranial Tumors of Different Histological Type" by S.K. Shapiro and his co-workers* calls for attention to the concurrent development of two primary intracranial tumors of diverse cell origin in an elderly patient. Despite the fact that glioblastoma and meningioma are the most common primary intracranial tumors of glial and non-glial cell origin, respectively in this old age group and their fortuitous association may be expected, their concurrent association presenting diagnostic problems as in this patient is indeed rare except in patients with von Recklinghausen's disease.

There have also been a number of reports describing the development of meningioma several to many years after surgical intervention and x-irradiation therapy for astrocytoma, oligodendroglioma, or pituitary adenoma. In these cases, the meningioma was located in or near the operative site and within the field of irradiation, and surgical trauma and/or x-irradiation have, therefore been incriminated as possible cause for the development of the meningioma.

The fact of further interest is that tumors of mesodermal cell origin such as fibrosarcoma, chondroma or chondrosarcoma may occur concurrently in contiguity with glioblastoma.

Joo Ho Sung, M.D.†
Minneapolis, Minnesota

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*Minnesota Med 59:2:84, 1976.

†Neuropathologist, University of Minnesota, Minneapolis.

Intractable Ascites

The procedure used by McMillen et al. in the February issue of MINNESOTA MEDICINE* and previously described by H. H. LeVeen[1] would appear to be a rather clever method of decompressing under local anesthesia the massively swollen ascitic abdomen of the cirrhotic patient. The operation should carry a low morbidity and mortality, but obviously must be carefully performed in order to avoid hemorrhage in the neck and infection around the catheter.

There is a real problem in keeping open prosthetic tubes in the lymphatic and venous channels —both low flow systems. It will be interesting to see whether McMillen's subsequent cases and followup will be as successful as his first.

However, it does seem that this procedure has merit in certain selected cases, and a further trial is indicated.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

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*Page 79.

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Letters to the Editor

We would like to encourage physicians to contribute to the Letters to the Editor Section. We want to hear what you have to say, what you think, why you hold certain opinions. In short, we want to make this as lively and spirited a section as possible.

The Editors

No. 3
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Treatment of Metabolic Alkalosis with Intravenous Hydrochloric Acid

METABOLIC ALKALOSIS with an arterial pH above 7.55 can produce cardiac dysfunction, tetany, seizures and shock. The usual therapy is removal of the cause, if possible, plus the administration of relatively large amounts of solutions containing sodium chloride and potassium chloride. If necessary, ammonium chloride, arginine hydrochloride or L-lysine monohydrochloride can be given. However, administration of these salts may be ineffective or contraindicated in the patient with hepatic and/or renal failure whose metabolic alkalosis is due to the continuing loss of large amounts of acid gastric fluid.

An effective answer to the problem is the intravenous administration of hydrochloric acid as described by Petzel, Masler, et al.* It can be given as an isotonic solution of 0.15 normal HCl (150 mEq HCl/liter) made by adding 150 ml of 1 normal HCl to 1 liter of sterile water. Dilute solutions of 0.05 to 0.1 normal HCl (50 to 100 mEq HCl/liter) can be added to 5% to 10% dextrose for infusion. The methods of calculating the chloride and hydrogen ion deficits to be corrected are described in reference 12 of the article by Petzel and associates. Administration usually is by central venous catheter to avoid irritation to peripheral veins. Blood pH and electrolytes should be monitored at six hour intervals during infusion of the hydrochloric acid.

On three or four occasions I have found the administration of 0.1 normal HCl in dextrose solution at a rate of 25 ml/hour plus replacement of gastric losses to be an effective method of relieving the tetany of metabolic alkalosis in the patient with acute oliguric renal failure treated by prolonged gastric suction. The stomach of the previously healthy patient with acute renal failure usually secretes considerably more HCl than does the gastric mucosa of the patient with chronic uremia.

Donald A. Duncan, M.D.
Minneapolis, Minnesota

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*See page 166.

First Hospital Accredited in Continuing Medical Education

North Memorial Hospital, Minneapolis, became the first Minnesota hospital to obtain accreditation as a sponsor of continuing medical education under the MSMA/AMA Accreditation Program. The MSMA Medical Education Committee, through its Subcommittee on Accreditation, has granted full accreditation status to North Memorial, thus officially recognizing the high quality of that hospital's programs in continuing education for physicians.

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6 + 6 + 1 = 13 . . . And if you take full advantage of the scientific program offerings at CME '76, 13 hours of continuing education will be yours for only $10 (non-members $25). It all adds up to Rochester, May 20-21.

Letters to the Editor

Dear Editor:

This message reports the success of reducing hypercholesterolemia in several patients by using Mazola oil, 2 tsp. given t.i.d., after meals. I would like to share the results on two patients that I have followed closely on this regime.

The first patient was 68 years old and had two heart attacks in the past three years. Her serum cholesterol was around 300 mgs%. On January 9, 1975 her cholesterol was 285 mgs%, and I started her on 2 tsp. of Mazola oil t.i.d. To my surprise and satisfaction on April 3, 1975 her cholesterol had come down to 250 mgs% and by September 27, 1975 her cholesterol was down to 199 mgs%. Her diet remained the same as before Mazola oil.

The second patient was 73 years old and had a myocardial infarction in 1962, and since then she has had several attacks of angina pectoris. On March 20, 1975 her serum cholesterol was 235 mgs%, and I started her on 2 tsp. Mazola oil t.i.d. On October 6, 1975 her cholesterol was down to 189 mgs%.

I have followed these two patients closely, and I do have other patients on the same regime that I do not check as regularly, but I certainly feel that this treatment is satisfactory. I also believe that I could have used any other polyunsaturated oil and had the same results.

George Friedell, M.D.
Minneapolis, Minnesota

Dear Editor:

Over the last two months I have tried, unsuccessfully, to implement Dr. Walsh's food allergy test procedure for atopic dermatitis*.

The mechanism whereby antigens reach the skin and cause exematous dermatitis mediated by type IV cellular, immunity (as seen with 48 hour patch tests) is reasonable. It has been demonstrated for many specific chemicals that are known to be in foods such as azo dyes and some spices as cinnamon.[1] The North American Contact Dermatitis group series of single standardized chemicals is presently available for the most common of these. If this series could be expanded to cover more food additives, it could prove useful in the management of "Atopic Dermatitis".[2]

I was unable to obtain useful results with Dr. Walsh's method of patch testing to over the counter food products. Control subjects included five women and one man without history of atopic dermatitis and one woman with a history of childhood exemia and no active lesions. Of patients tested there were: (1) eighteen with flexural exematous and lichenified dermatitis who had been followed for several years, (2) two with similar pattern of dermatitis who were tested on their initial visit, but had long histories of similar involvement and (3) five patients with recurrent hand exemia which were previously shown to be unresponsive to the North American series.

As suggested, foods were purchased at local stores and consisted of coffee, powdered milk, cocoa, and wheat flower. Ten percent citric acid in aqueous solution was prepared. Formula used in feeding some of the infants was also patch tested in four children.

Patch tests were performed by Dr. Fischer for testing unstandardized substances.[1]

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*Minnesota Med 58:4, 1975.

Patch tests were remarkably negative. One patient performed heavy exercise while wearing the patches and developed miliarial eruption under the entire covered area. Repeat testing in this subject was negative. One patient, who described perioral exematous dermatitis from oranges, showed a 3+ reaction to citric acid. Avoiding citric acid over one month did not alter the flexural exematous dermatitis.

Joel T. M. Bamford, M.D.
Duluth, Minnesota

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Cover Photo

"Minnesota at Gettysburg"

On the 2nd of July, 1863, the First Minnesota regiment, numbering 262 officers and men, commanded by Colonel William Colvill of Red Wing, Minnesota, was ordered by General Winfield S. Hancock on a suicide mission to stem a confederate charge on Cemetary Ridge. Within fifteen minutes 215 of the 262 men of the regiment lay dead or wounded. (The 82% casualty is usually cited as the largest suffered by any regiment in the entire war.) The remaining few stemmed the charge. Reserves arrived, and the Union Center was saved. This is the Minnesota Monument to these brave men and is located at Gettysburg.

Dr. Julien V. Petit, who took the cover photograph, is a 57-year-old physician practicing internal medicine in Minneapolis. The January, 1975, issue of MINNESOTA MEDICINE has for its cover another of Dr. Petit's photographs.

Accreditation of Programs in Continuing Medical Education

The Minnesota State Medical Association has begun the process of accrediting Minnesota hospitals and other organizations sponsoring programs in Continuing Medical Education for physicians. It is the intent of the MSMA to accredit the sponsoring organizations for all of their ongoing CME activities and not the individual courses and programs. As the system of accreditation becomes fully operational, all hospitals and medical specialty societies in the state will be notified how to apply. Meanwhile, your questions should be directed to Paul F. Bowlin, M.D., Chairman, Accreditation Subcommittee, in care of the MSMA office.

Inquiries concerning any other aspect of the CME program may be directed to the MSMA office in care of Dr. John S. Welch, Chairman of the Medical Education Committee.

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Ramsey County Medical Society

What's Right with Medicine?*

To begin on a positive note. Other than Harry Schwartz and our families, medicine doesn't have many visible outside supporters. I feel it is proper to ask "what is *right* with medicine?" Many of us have become defensive and downright paranoiac—it seems nothing we do is right—at least according to our detractors.

Let me tell you why I am still excited about being a physician. I'm sure you all could add many more.

The excitement of attending at a birth—to witness the mother's suffering turned to joy, the father's anxiety turned to pride, the miracle of life. To observe the growth of that child from infancy, to teenage, to young adulthood and for older physicians, the delivery of that child's children.

To work with colleagues of superior skill, knowledge, wisdom, competence and interests. To watch and listen to gifted teachers amongst us who share their wisdom with our bright and eager young physicians, medical students and associates.

To practice medicine in a time of marvelous advances—in research, both clinical and laboratory—the vaccines, antibiotics, the tools available, the surgical frontiers conquered.

The satisfaction of solving a difficult diagnostic puzzle; discovering a lesion the repair or removal of which allows prolongation of life; and particularly for me, the challenge of a difficult alcoholism problem and successful recovery that keeps a family together, prevents further physical, mental, financial and moral deterioration and allows the patient to develop an inner peace, love of life and his fellow man.

The amount of preventive medicine we practice—prenatal care, well baby care, periodic physicals, immunizations, proctos, blood pressure checks, sports physicals, pelvic and pap exams, urinalysis, etc.

The physician's sense of duty and dedication. The high ethical standards of medicine and physicians.

The competitive drive physicians show to keep up or excel through refresher courses, individual reading, and other forms of continuing education even before it became publicly popular.

To share the trust and confidence of our patients. The amount of free care given by physicians unbeknownst to most.

Having witnessed many politico-medical discussions, the sincere concern expressed by my fellow physicians not only for his/her welfare but the welfare of his/her patients, community and society as a whole.

The privilege of being able to study the human body in medical school and to marvel at the function and repair processes of this wonderful creation of God as we proceed through our medical careers—so much of which we understand—so much more we don't.

Finally, the kindness, dignity, compassion and understanding most of my associates show to the living, the troubled and the dying.

I am proud to be a physician—and have you for a colleague.

Thomas G. Briggs, M.D.
President

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*From Ramsey County Medical Society Bulletin, January, 1976. By permission of author and society.

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Dryness of Mouth and Eyes

A 58-year-old white woman presented with the history of dryness of mouth and redness and burning of eyes for many years. There had been no joint pains. Positive physical findings were a palpable spleen, bilateral keratoconjunctivitis sicca, and petechia on both legs. Laboratory examinations disclosed a microcytic normochromic anemia with a Hgb level of 11.1 gm%. W.b.c. 1700/cmm, neutrophils 34%, lymphocytes 61%, monocytes 5%. Platelets 204,000/cmm, ESR 41 cmm. Routine blood chemistries normal. Rheumatoid factor positive at 1:320.

Sequential scintigraphy of the salivary glands was performed using 10 millicuries of sodium pertechnetate Tc^{99m} (Figures 1A and 1B).

What is your diagnosis? See next page.

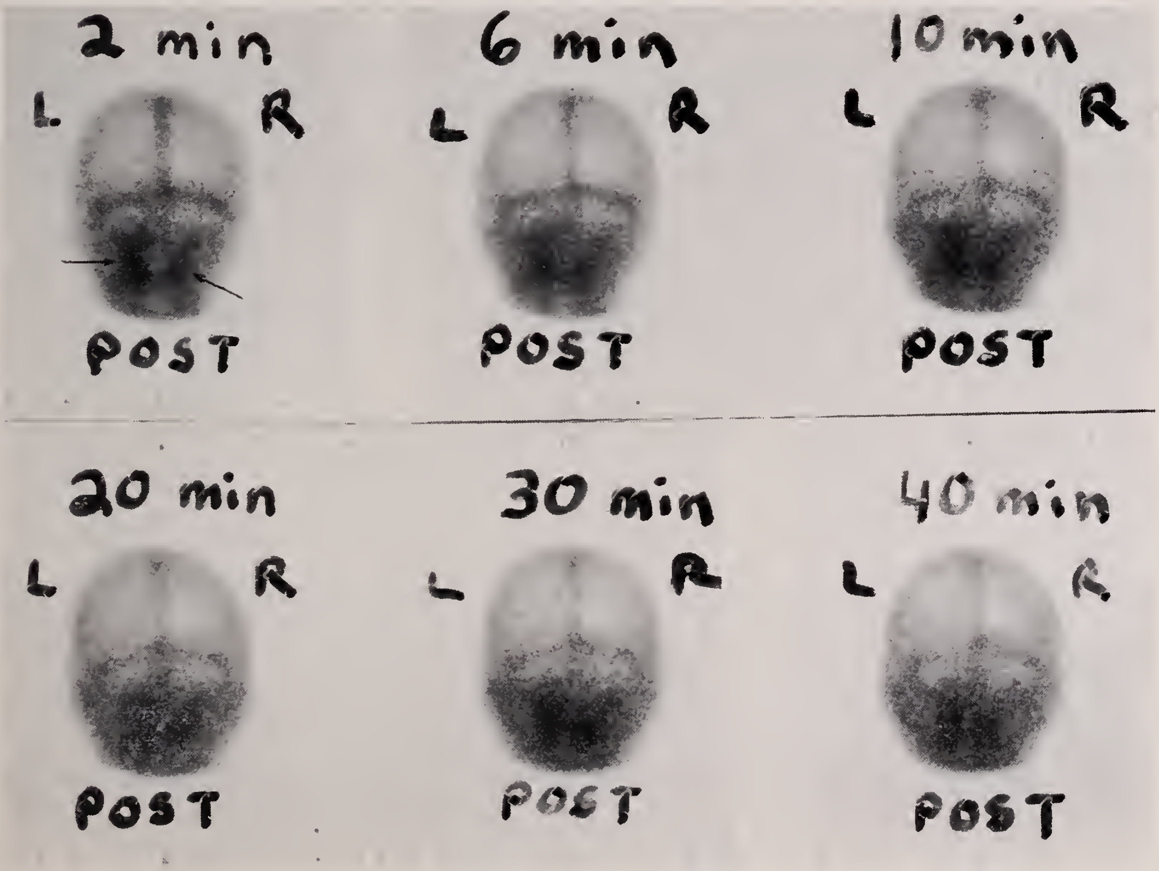

Figure 1A

Diagnosis: Sjögren's syndrome with xerostomia

The pertechnetate anion is actively concentrated in the salivary glands at the ductular level and then excreted into the saliva. Scintigraphy of normal glands discloses intraglandular accumulation of radioactivity within 10′ after the intravenous administration of the tracer, followed by progressive increase in concentration and prompt excretion into the oral cavity by 20—30′. At 60—80′ the oral activity is greater than that in the glands.

In the present case radioactivity was demonstrated in the submandibular glands (arrows) at 2′ without subsequent rise (Figure 1B—short arrows). The left gland was enlarged. Definite parotid activity did not appear until 60′. The functioning parenchyma of the left parotid gland was small. Oral activity was absent even at 80′ (long arrow). These findings indicate severe functional impairment of the salivary glands with xerostomia.

Sjögren's syndrome can be diagnosed when any two of its three components, i.e., xerophthalemia, xerostomia and chronic arthritis are present. This patient had keratoconjunctivitis sicca and xerostomia, which was confirmed by salivary scintigraphy. Splenomegaly, granulocytopenia, thrombocytopenia, and elevated erythrocyte sedimentation rate are some of the associated features of the syndrome. The test for rheumatoid factor is positive in almost all cases.

Sequential imaging of the salivary glands following the I.V. injection of Tc^{99m} pertechnetate is a simple, safe, and non-invasive method of evaluating their function and their sizes. Schall et. al. reported that, in a series of 20 patients with

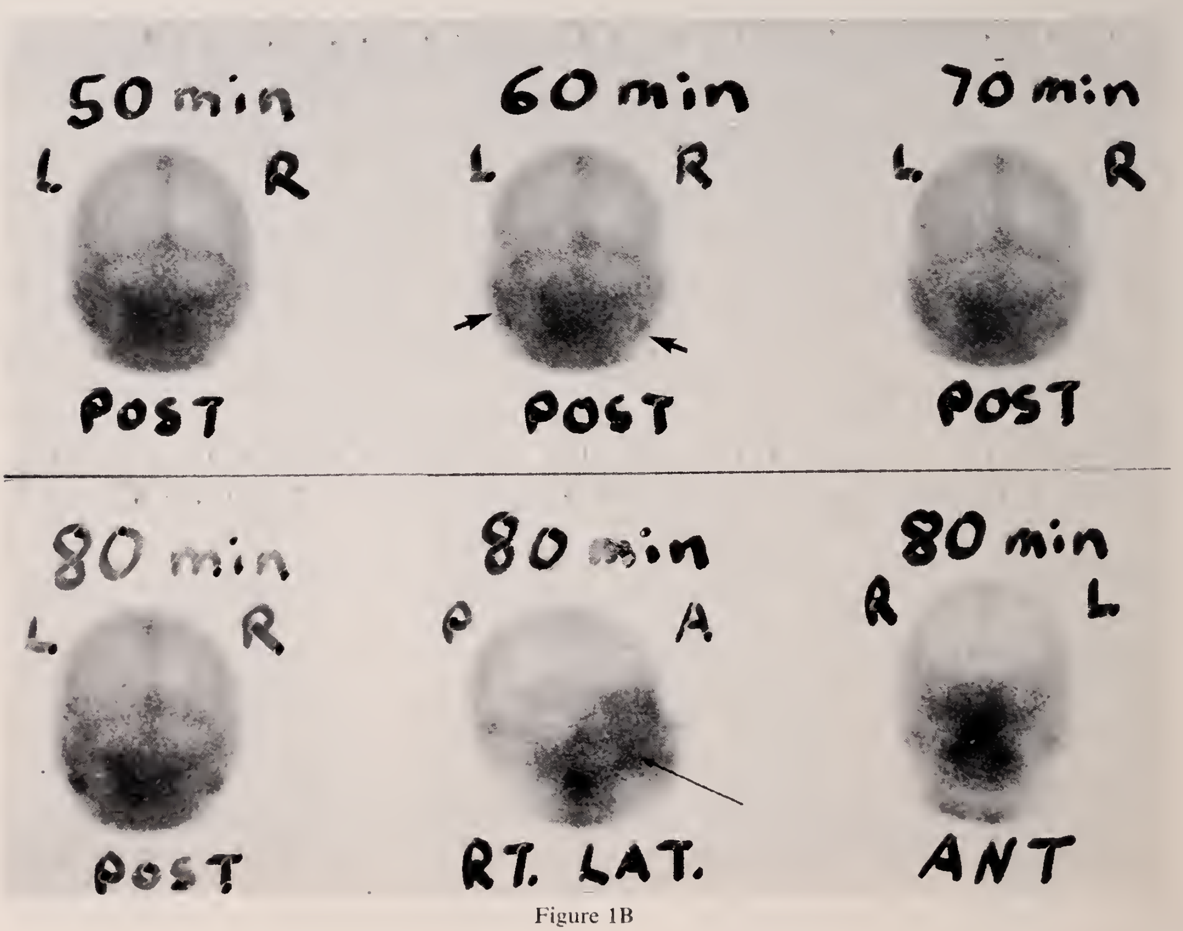

Figure 1B

the Sjögren's syndrome, the scintigraphic findings correlated closely with the results of salivary flow-rate determination and contrast sialography and the clinical symptoms, but not with those of lip biopsies and anti-salivary-duct antibody determinations. They found scintigraphy extremely sensitive in depicting small asymmetrical differences in glandular function and therapeutic response of the glands to immunosuppressive drugs. They also pointed out that the scintigraphic evidence of salivary gland dysfunction is nonspecific, and, by itself, is not diagnostic of the Sjögren syndrome.

Scintigraphy may also be useful in the evaluation of tumors, cysts, and inflammatory diseases of the salivary glands.

The radiation dose from 10 millicuries of Tc^{99m} pertechnetate is estimated to be 0.12 rads to the whole body, 1.13 rads to the colon (critical organ) and 0.6 rads to the normal parotid gland. It will be less to a gland that concentrates the tracer poorly.

S. H. Tsai, M.D.*
Minneapolis, Minnesota

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*Department of Radiology, Hennepin County Medical Center, Minneapolis, Minnesota.

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Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

1. Preferably an alumnus of the University of Minnesota Medical School.
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Nominations for the 1976 awards should be sent immediately to:

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Review

Transfusion Review in Minnesota Hospitals

JOHN O. SWANSON, M.D.[*] and HERBERT F. POLESKY, M.D.[†]

Transfusion review practices of forty-six Minnesota hospitals are described. We include suggestions for hospital transfusion committees relative to committee make-up, topics for review, and sources of data. Emphasis is placed on the use of the review process as a tool for education of the medical staff.

BLOOD AND BLOOD components are therapeutic agents available in limited quantities which, though life saving when used appropriately, have a significant risk of transmitting disease. It has been demonstrated by Walz[1] and Crosby[2] that periodic peer review of transfusion practices when combined with an education program can lead to significant improvement in patient care. With the advent of the National Blood Policy and its emphasis on efficient management of the blood resource, we decided to survey Minnesota hospitals to determine how and to what extent blood utilization is monitored.

Method

In April, 1974, we contacted pathologists in fifty-one of the larger Minnesota hospitals, requesting information about the transfusion review practices of their institutions. There were forty-six (90%) responses.

Results

Who Is Doing The Review?

Twenty-five of the forty-six hospitals surveyed have transfusion committees (Table 1). A majority of these are actually tissue and transfusion committees. One pathologist notes that 99% of his committee's work deals with tissue review and 1% concerns transfusion practices.

Of the twenty-one hospitals without a formal transfusion committee, three have no transfusion review. Pathologists of two of the smaller hospitals review each transfusion; one reports to the executive committee each month. In the other sixteen hospitals, transfusions are reviewed by a variety of groups (Table 1). Pathologists from several of these sixteen hospitals state that their transfusion review is almost non-existant.

How Often Are Transfusions Reviewed?

Frequency of review is variable (Table 1). Some hospitals review transfusion practices conscientiously and regularly. Many others review transfusions infrequently, "if there is time" or "if a problem exists." According to our survey, some of those who regularly review transfusions as a function of another committee allow very little time for this subject.

What Is Being Reviewed?

The American Medical Association Guide for Hospital Committees on Transfusion suggests that the committee assure the hospital of a safe, adequate supply of appropriately used blood and components.[3] The topics (Table 2) considered by hospitals responding to the survey indicate that

TABLE 1
Review of Transfusions in 46 Minnesota Hospitals

		Frequency		
	No.	At least every 6 mo.	6-12 mo.	Yearly
Transfusion Committee	25	16	3	3
Pathologist	2	2		
Other Committee	16	6	6	4
ClinicalSection Meetings	3			
Medical Audit Committee	4			
Patient Care Committee	4			
Tissue and Surgery Committee	4			
Utilization Review Committee	1			
No Review	3			
Total	46	24	9	7

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[*] Pathologist, Metropolitan Medical Center, Minneapolis, Minnesota.

[†] Director, War Memorial Blood Bank, Minneapolis, Minnesota.

TABLE 2
Topics Reviewed by Committees

Transfusion Reactions	20
Single Unit Transfusions	17
Component Therapy	15
Indications	14
All Transfusions	11
PAS-MAP Data	7
Statistics	6
Transfusion Hepatitis	5
Problems	5
Policy	2

these guidelines are being followed. Several transfusion committees also formulate hospital transfusion service policy and rules.

To Whom Are Reports Made?

Table 3 lists the recipients of the transfusion committee reports. Those transfusion committees which report to the medical audit or patient care committees are two steps away from the governing medical executive committee and three steps away from the medical staff. From one point of view, the greater the number of committees which hear the transfusion review, the better. In fact, the more interceptions of the transfusion report before it reaches the medical staff, the less likely it is to receive a hearing by most of those who transfuse patients.

TABLE 3
Transfusion Committee Reports To

Medical Staff Only	4
Executive Committee	14
Medical Audit	3
Patient Care	1
Surgical Committee	1
Not Answered	3

What Problems Were Identified?

From information gathered in this survey and from personal experience with transfusion committees, some problems are apparent. The first is organizing the reviewing group and the reviewing process. A second problem is the agenda; a third is data collection for the meetings. Finally, and perhaps the most troublesome of all, there is the sensitive area of enforcement of policies and rules, and the problem of how we get the reviewed information to the medical staff for educational purposes.

Discussion

Why Bother?

Why review transfusions at all? First, a review audits an important aspect of medical practice. Walz states that "a transfusion committee, with a cooperative staff, can make significant improvements in transfusion practices."[1] A second reason for review is its education value, assuming the reviewed data finds its way to the medical staff. Crosby writes that "The Hospital Transfusion Board provides an educational method which, if properly implemented and motivated, can improve both the therapeutic effectiveness and the economy of a hospital transfusion service."[2] Medicare and Joint Commission on Accreditation of Hospitals requirements and medical-legal considerations are additional reasons for evaluating transfusion practice.[4,5] Okuno writes that the Cunningham case, in which a hospital was held strictly liable to a patient who allegedly contracted hepatitis after a blood transfusion, "has played a decisive role in the changes of trends of blood usage. The impact by the case has been far greater than that by various educational activities hitherto undertaken in our hospital."[6]

Who Should Do the Review?

Transfusion policy and practice should be reviewed by the group or committee best suited for and most interested in the task.

The AMA Guide states that the "character and size of the hospital and its staff will determine the makeup of the transfusion committee."[3] A physician appointed to the committee must have an interest in this area, and must be willing to donate a small amount of his time. In some hospitals, there is the problem of: (1) getting the physician members to come; and (2) getting the physician members to sit through the meeting. Brevity and a well-organized agenda go a long way toward encouraging attendance and attention.

As an alternative to a formal transfusion committee, several hospitals in Minnesota are doing an outstanding job of monitoring transfusion therapy by reviewing this subject regularly at clinical section meetings. Cases are reviewed and discussed. Statistics for usage and component therapy are impressive in these hospitals.

The role of the pathologist in transfusion review varies, depending upon the institution. Some favor a dominant role by a pathologist; others favor little or no involvement by the pathology staff except to serve as consultants to the committee or reviewing group.[7] Either way, reviews tend to be more effective when clinicians are actively involved.

What Should Be Reviewed?

William Crosby writes that the transfusion committee has the "responsibility to investigate all phases of the transfusion service and to recommend appropriate action."[2] Historically, transfusion reviews have concentrated on single unit transfusions, sometimes to the exclusion of all else. We suggest concentrating on "total correct blood usage,"[1] with the one unit data as only one of a number of indicators of such usage.[8,9] Crosby writes that "there are valid indications for transfusing a single unit of blood and no more." "Sometimes it demonstrates an unusual skill in the use of transfusion as a therapeutic tool. At other times it is an act of thoughtlessness or incompetence."[10] In an editorial in the New England Journal of Medicine, entitled *The Case for the Single Transfusion,* J. Garrott Allen writes that "if transfusion committees are to monitor the use of single transfusions as an index of good practice, they need to know not only the number of single transfusions administered, and the circumstances under which they were given, but the numbers of two's, three's and four's as well . . . Deletion of one transfusion at any level is the important principle to achieve—not just the one unit case."[11]

Where To Find Data

Data for a review meeting may be obtained from three sources:

(A) The PAS-MAP provides information about the number of patients transfused with whole blood, packed cells, and plasma products for many diagnostic categories, the number of one unit and two unit transfusions, the diagnosis and admission hemoglobin for patients who receive blood products, and the number of patients transfused with an admission hemoglobin of less than 10 grams and over 14 grams/dl.[12] One of the advantages of this system is the ease with which specific cases may be selected for detailed review.

(B) The blood products supplier (blood donor center) also has data and statistics for each supplied facility.

(C) The hospital blood bank and the hospital laboratory computer records will provide information for review, such as the number of components used, transfusion reactions, and the incidence of transfusion-related hepatitis. Records are more usable if they are kept current.

The Goal of the Review Process

The goal of the committee should be better patient care. Ideally, education of the medical staff will accomplish this goal. From time to time it may be necessary to firmly enforce the policies established by the reviewing body.

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Laboratory Medicine

Should You Add PEP to Your Office Lab?

RICHARD M. STEIDL, M.D.[*]

FEDERAL REGULATIONS applying to medical practice are emanating from Washington like nocuous gases from a primordial ooze. However much we may consider them as infringements on our right of private practice, they are a fact of life, which should be anticipated and prepared for because they can not be ignored. A case in point is the proposed Clinical Laboratory Improvement Act of 1975 (CLIA '75). The Senate version of this bill is jointly sponsored by Senators Kennedy and Javitz, who held hearings on the bill on September 8-9, 1975. At that time Senator Jacob Javitz[†] left no doubt that he planned to include the monitoring of physicians' office laboratories in the bill. How monitoring of as many as 80,000 office laboratories would be carried out has not been explained. Senator Javitz has suggested that physicians might have to sign statements relating to the maintenance of an up-to-date procedure manual, certain operating and personnel records, and participation in an approved proficiency testing program. HEW has suggested that it can influence office laboratories by setting up standards for materials, kits and equipment under the authority of the Food and Drug Administration.

The House version of the bill, to be introduced by Representative Paul Rogers[‡] will have hearings during the coming year. The bill, similar to the Senate version, subjects all laboratories, including independent, hospital and doctor-office laboratories, to licensing.

Although it is yet too early to determine what the final form of the bill will be, it appears inevitable that all laboratories will be subject to some form of accreditation.

To compound the problem for the practicing physician is the additional legislation which has either been passed or is pending at the state level. California, Arizona and Maryland currently require proficiency testing. Illinois will soon follow, and bills are pending in other state legislatures.

Finally, current Medicare regulations require that any physicians' office laboratory which performs 100 tests or more on a referral basis, in any one category, must participate in a proficiency testing program.

From the foregoing, it appears that some form of proficiency testing will be required by all laboratories within the near future. It should be noted that the CLIA '75 states that a "laboratory may participate in any proficiency testing program that is acceptable to the Secretary." Recognizing the inevitability of legislation related to physicians' laboratories, it seems prudent to initiate a program of quality control within physicians' office laboratories, so that a continuity of service may be provided once the federal mandate becomes a fact of life.

In 1969, the College of American Pathologists[#], under the able leadership of Dr. Raymond Hain, developed the Proficiency Evaluation Program (PEP) to permit our clinical colleagues to achieve a higher level of performance within their laboratories. It was an altruistic program designed not only to identify problems within the laboratory, but also to provide through literature and local consultations, for the resolution of such problems. In order to guarantee that the interests and needs of their clinical colleagues would be well served, the College of American Pathologists invited the American College of Physicians and the American Academy of Family Practice each to appoint a representative to work with the four clinical pathologists on the PEP committee. These representatives have had a positive input into the plans and programs of the committee.

The PEP program has been endorsed both by the American Academy of Family Practice and the American College of Physicians. The Education Commission of the Minnesota Academy of Family Physicians has also recommended to its members that they participate in this program. The Minnesota Society of Clinical Pathologists has set up a committee to act as a liaison between the MSCP and the MAFP.

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PEP, offers the following specific benefits:

- . . . An outside quality control check on the results of your office laboratories system.
- . . . A peer control evaluation against hundreds of other physicians' office laboratories employing the same methods, instruments and reagents.
- . . . A check on possible sources of error.
- . . . A listing of local consultants who are willing to assist you in your laboratory to resolve any technical or procedural problems,
- . . . An extra measure of assurance concerning the laboratory values upon which you base your patient care decisions.
- . . . Hour-for-hour Category I credits toward the AMA Physician Recognition Award.

The program provides confidential data to assist in evaluating the performance of your laboratory and meets the requirements of current State and Federal legislation. At the personal request of the participating physician, the College of American Pathologists will forward a copy of the results to a state-certifying agency, *but only if the participant has given prior written authorization for such forwarding.*

In conclusion, adding a little PEP to your office laboratory will not only meet demands for quality control being written into legislation such as the CLIA '75, but, more important, will result in greater confidence in the laboratory results generated. The end result can only be better care for your patients.

Continuing Education

Prosthetics and Orthotics

A regional training program in prosthetics and orthotics will be held at the Holiday Inn (Downtown), Minneapolis, Minnesota on March 11 through 14, 1976, under the joint sponsorship of the Research Center for Prosthetics, New York, New York, and the Minnesota Chapter of the AAOP. The Minneapolis VA Hospital will be the host station. Registration fee is $20.00. Please address inquiries for information and/or registration materials to R. O. Wood, 4438 Wentworth Avenue South, Minneapolis, Minnesota 55409.

Pediatric Day Sponsored by the Mayo Clinic

Pediatric Day sponsored by the Mayo Clinic will be held March 12, 1976. The Amberg-Helmholz Lecture, a feature of Pediatric Day, will be given by Barbara M. Korsch, M.D., of the Children's Hospital of Los Angeles. Presentations dealing with problems which occur in the practice of Pediatrics will be made by members of the staff of the Mayo Clinic. For information, write Doctor E. Omer Burgert, Program Director, Mayo Clinic, Rochester, Minnesota 55901.

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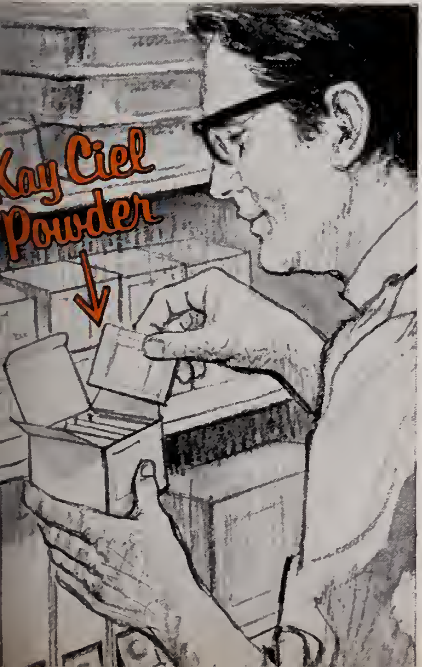
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Testing in Humans: Who, Where & When.

e weight of ethical opinion:

Few would disagree that the effective-
ss and safety of any therapeutic agent
device must be determined through
nical research.

But now the *practice* of clinical re-
rch is under appraisal by Congress, the
ss and the general public. Who shall
minister it? On whom are the products
be tested? Under what circumstances?
d how shall results be evaluated and
ilized?

The Pharmaceutical Manufacturers
sociation represents firms that are sig-
ficantly engaged in the discovery and
velopment of new medicines, medical
vices and diagnostic products. Clinical
search is essential to their efforts. Con-
quently, PMA formulated positions
hich it submitted on July 11, 1975, to
e Subcommittee on Health of the Sen-
e Labor and Public Welfare Committee,
its official policy recommendations.
ere are the essentials of PMA's current
inking in this vital area.

1. PMA supports the mandate and
ission of the National Commission for
e Protection of Human Subjects of
iomedical and Behavioral Research and
fers to establish a special committee
mposed of experts of appropriate
sciplines familiar with the industry's
search methodology to volunteer its
rvice to the Commission.

2. PMA supports the formation of an
dependent, expert, broadly based and
presentative panel to assess the current
ate of drug innovation and the impact
on it of existing laws, regulations and
rocedures.

3. When FDA proposes regulations,
should prepare and publish in the *Fed-*
al Register a detailed statement assess-
g the impact of those regulations on
ug and device innovation.

4. PMA proposes that an appropri-
ely qualified medical organization be
couraged to undertake a comprehen-
ve study of the optimum roles and
sponsibilities of the sponsor and physi-
an when company-sponsored clinical
search is performed by independent
inical investigators.

5. PMA recognizes that the physician-investigator has, and should have, the ultimate responsibility for deciding the substance and form of the informed consent to be obtained. However, PMA recommends that the sponsor of the experiment aid the investigator in discharging this important responsibility by providing (1) a document detailing the investigator's responsibilities under FDA regulations with regard to patient consent, and (2) a written description of the relevant facts about the investigational item to be studied, in comprehensible lay language.

6. In the case of children, the sponsor must require that informed consent be obtained from a legally appropriate representative of the participant. Voluntary consent of an older child, who may be capable of understanding, in addition to that of a parent, guardian or other legally responsible person, is advisable. Safety of the drug or device shall have been assessed in adult populations prior to use in children.

7. PMA endorses the general principle that, in the case of the mentally infirm, consent should be sought from both an understanding subject and from a parent or guardian, or in their absence, another legally responsible person.

8. Pharmaceutical manufacturers sponsoring investigations in prisons must take all reasonable care to assure that the facilities and personnel used in the conduct of the investigations are suitable for the protection of participants, and for the avoidance of coercion, with a respect for basic humanitarian principles.

9. Sponsors intending to conduct non-therapeutic clinical trials through the participation of employee volunteers should expand the membership and scope of its existing Medical Research Committee, or establish such an internal Medical Research Committee, with responsibility to approve the consent forms of all volunteers, designs, protocols and the scope of the trial. The Committee should also bear responsibility to ensure full compliance with all procedures intended to protect employee volunteers' rights.

10. Where the sponsor obtains medical information or data on individuals, it shall be accorded the same confidential status as provided in codes of ethics governing health care professionals.

11. PMA and its member firms accept responsibility to aid and encourage appropriate follow-up of human subjects who have received investigational products that cause latent toxicity in animals or, during their use in clinical investigation, are found to cause unexpected and serious adverse effects.

12. PMA supports the exploration and development by its member companies of more systematic surveillance procedures for newly marketed products.

13. When a pharmaceutical manufacturer concludes, on the basis of early clinical trials of a basic new agent, that a new drug application is likely to be submitted, a proposed development plan accompanied by a summary of existing data, would be submitted to the FDA. Following a review of this submission, the FDA, and its Advisory Committee where appropriate, would meet with the sponsor to discuss the development plan. No *formal* FDA approval should be required at this stage. Rather, the emphasis should be on identification of potential problems and questions for the sponsor's further study and resolution as the program develops.

The PMA believes that health professionals as well as the public at large should be made aware of these 13 points in its Policy on Clinical Research. For these recommendations envisage constructive, cooperative action by industry, research institutions, the health professions and government to encourage creative and workable responses to issues involved in the clinical investigation of new products.

P·M·A

Pharmaceutical Manufacturers
Association
1155 Fifteenth Street, N.W.
Washington, D. C. 20005

Special Article

The Philosophy Of Preventive Medicine

JOHN E. SMITH, M.D.*

Whether you pay in advance (HMO) or later, medical care is a service given by someone to someone, and the more you get the more it costs. With the right to health care goes the responsibility to care for your health. Preventive medicine is something you do, not something you get. The example of physicians practicing good health habits would benefit those physicians directly and their patients indirectly.

DOCTORS ARE BEING widely criticized for care that is episodic rather than comprehensive, treatment focused rather than preventive. In short, for placing too much emphasis on the here and now and too little on the future. Part of this is because doctors get their pleasure from making people feel better, and it's hard to make an asymptomatic patient feel better. A physician's *financial* reward is often delayed, but some things like putting a catheter in a distended bladder or washing out a wax filled ear or removing a sliver, give instant relief to a grateful patient and the reward is immediate.

In practice, however, the present and the future blur together. Giving Penicillin for a Strep Throat both treats an acute infection and prevents future complications. An incidental Appendectomy done in the course of other surgery prevents an attack of Appendicitis in the future but is done in the context of treating present disease. A dentist repairing a cavity certainly prevents future more serious dental problems, and yet is giving acute care.

Doctors Cannot Maintain Health

Doctors and medicine have been oversold; good health is not ours to sell. Our knowledge and expertise are inadequate; the present state of our art is incomplete. With a few outstanding exceptions we cannot prevent disease; we cannot maintain health; only sometimes can we postpone dying. Until we learn how to do these things, we do what we can by giving acute, episodic care to sick people. Even this is straining the resources of our system, both medical and financial.

If you add to this already strained system the need to do somthing for healthy people (preventive medicine), it will add to the cost and fill our offices with the well and the worried well. There will be no room for those who really need a doctor. It is bad enough even now when financial incentives tend to keep patients out of the office. We must work to develop more effective incentives to be used to motivate *all* participants to *use* and *provide* health services prudently and efficiently.

HMOs Cannot Maintain Health

Just as doctors cannot maintain health, so is it impossible for organizations to maintain health. The term Health Maintenance Organizations (HMOs) is a promise that can't be delivered. HMOs are simply a way of paying in advance for medical care, a way that allows budgeting a fixed yearly fee. The worst thing about them is that they reward the doctor for *not* doing something, where the fee-for-service practice rewards the doctor for doing something. The danger of doing is called overutilization which harms the pocketbook. The danger of not doing is called underutilization and it harms the patient. Just because you keep someone out of the hospital doesn't mean that you have kept him well; all it means is that for whatever reason, you haven't put him in the hospital.

Trying to Keep People Well Costs Money

HMOs can take care of a given part of the population at less cost by denying or delaying coverage for that majority of medical and surgical care which lies in the zone of desirable but not essential. HMOs can also keep the costs down by enrolling only working people and their families. But one way HMOs cannot save money is by practicing preventive medicine. Preventive medicine costs money and except for primary prevention (immunizations) there are no proven cost effective programs for the primary physician to perform.

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*Minneapolis, Minn.

Anything can be done cheaper, but trying to keep people well costs money. If the main effort of the system is to save money, then the younger you are when you die the more money you have saved. Postponing death (prolonging life) usually has much to recommend it from the point of view of the individual, but it costs money and the more care you get the more it costs.

Public Health Medicine

Nevertheless, there are extremely cost effective kinds of preventive medicine. Most of our prolongation of life can be attributed to *Social* medicine which concerns such matters as food, housing, transportation, law enforcement, etc. A second contributor to longevity is *public health medicine* which features broad, impersonal approaches to problems such as sanitation, rodent and insect control, garbage disposal, food inspecton, pollution, quarantine, and keeping the sewer pipes separate from the drinking water.

Early Detection of Disease

Early detection of disease, which is the hope behind both the health screening profile and the periodic physical exam, should help prevent the complications of more extensive disease but there is disagreement on this. One author[1] has come to the conclusion that "screening is worthwhile for only six conditions; dislocation of the hip and phenyl-ketonuria in neonates; hearing and vision in preschoolers; Rh factor and bacteriuria in pregnant women." Many are certain that for some additional things like detection of cervical cancer (pap smear) screening has proven valuable.

For some other conditions, screening has been a mixed blessing. The current emphasis on detecting asymptomatic hypertension has been effective and statistics seem to indicate that early treatment will prevent later complications, but it is hard to get asymptomatic patients to take medications, especially when that medication may make them feel worse.

There are conditions like an elevated Cholesterol that are easy to detect—which we know put the patient at increased risk—and which we can successfully treat, but no one has ever proven that lowering the Cholesterol in these patients influences their life expectancy. Some studies have shown that in asymptomatic Diabetes early treatment actually increases the risk of complications. Early detection of disease may not make people live longer, but it will let us classify them as "sick" longer. This, of course, is no benefit. In most ways it is better to die thinking you are going to live, than to live thinking that you are going to die.

Glaucoma screening and proctoscopic exams in older people are valuable procedures in those few (9 per 55,000) individuals with the disease, but are only slightly more cost effective for the general population than are the mobile chest Xrays (two per 35,000) which have been abandoned.[2]

There are some diseases like Phenylketonuria, that are so rare I'm never going to find a case (one per 10,000 live births) and yet most states have passed mandatory screening laws. By implication, treatment has also become mandatory; yet PKU is a complex disease state whose management calls for much more knowledge than is now available. Sickle Cell Disease is an example of another currently popular crusade, for which screening programs are being enthusiastically endorsed and for which the only useful intervention is *prior* genetic counseling.

Critical Questions

For all screening programs we have to answer the following questions: What is the likelihood that the screening test will be abnormal? What is the likelihood that the abnormal test will indicate disease? Can we treat the disease if discovered? Is the treatment worse than the disease? What is the likelihood that an asymptomatic patient will accept treatment?

Complete Physical Examination

The main benefit of a periodic physical exam is the opportunity for the doctor and the patient to learn to work together. The examination has considerable psychotherapeutic value, and it is an opportunity for the old fashioned "laying on of hands." It also serves as an opportunity for patient education, for the end of the exam—the point of prescription—is a true teachable moment. The worst thing about periodic physicals is that they encourage the belief that physicians can prevent disease.

The annual executive physical is a peculiarly American institution and serves a secondary purpose of emphasizing the pecking order within a company. The more money the company is willing to spend on your exam the more valuable you are to the company. To advocate complete annual exams for all patients would be an absurdity. It would require the entire medical budget and all of the time of all of the doctors. There would be no resources left to treat sick people.

There is no such thing as a "complete physical exam" anyway. We never do all the tests known to man. We don't test for all diseases which it is possible to get. We tailor our exam and our testing to probabilities, and then try to motivate people to modify their habits in ways that will favorably affect their life expectancy.

Multiphasic Screening

While early detection of disease through the periodic physical exam has those limited benefits, trying to accomplish the same thing through multiphasic health testing (ala Kaiser in California) is even one more step removed from reality. The main things the multichannel testing accomplishes is to generate medical busywork. It sometimes does detect unsuspected disease but it as often involves us in the early detection and treatment of non-disease. This is extraordinarily wasteful. As Gertrude Stein said, "a difference to be a difference must make a difference."

An elevated Uric Acid has always been a part of our diagnosis of Gout, but with screening chemistry profiles we have been finding elevated Uric Acids in asymptomatic people. Is this Hyperuricemia the same as Gout; is it a warning that Gout is coming; or it is meaningless? Should we treat it or ignore it? Hypoglycemia is another popular non-disease which can be used to explain a variety of symptoms. Its diagnosis and treatment would be better left undone.

In a twelve channel screen chemistry test 46% of *NORMAL* people will have at least one test fall outside the normal range. With a 22 channel screen, 66% of normal people will have at least one abnormal test.[8] Even if you don't treat these abnormal tests, just doing further testing to decide whether it is a normal variation is a waste of time and money.

Primary Prevention

Primary prevention, however, is the essence of preventive medicine. This is a specific service to ward off a specific disease and its prototype is immunization. Its benefits in many infectious diseases are well known. A vaccine to prevent cancer would be a boon to all mankind; but a doctor is not needed to give the shots. The great benefits from social and public health medicine have already been accomplished; they are no longer the concern of primary physicians. Machines can continue to do the periodic health screening even though they are costly and of limited effectiveness. Physicians' assistants can be taught to do the physical exams, and health educators may do a better job in teaching patients about their diseases. In fact there isn't anything doctors do that we couldn't train someone else to do as well.

What, then, is left for the physician to do? Only that which he has always done best—giving acute, episodic care to sick people. That and trying to co-ordinate all the other parts of the system into a comprehensive whole. That and trying to learn how to motivate and educate people to self-medicine, self-prevention and a change in life style; for herein lies the real philosophy of prevention.

I know of one HMO Plan where they force compliance in Health Maintenance by kicking all those out of the plan who won't stop smoking, lose weight, get regular exercise, take their medicine, have regular checkups, stop drinking, etc. Now there is real motivation.

But you can't force people to do what's best for them. Even for indicated and necessary surgery the final authorization has to come from the patient. People have to be free to make the wrong choice if that is what they want. I agree with this laissez-faire philosophy of prevention, and it is summed up by a sign I had over my bar at home; "If you drink wine you have the Gout. If you don't drink wine the gout has you."

Self Medicine

Self medicine is the facet of prevention with the greatest impact on our future, but programs for self-health maintenance are difficult to devise and maintain. Education is not the whole answer. Even Cardiologists die of heart disease. Yet there are reasonable and acceptable alternatives to the American Way of Life. We must learn how to motivate our patients toward these alternatives of decreasing alcohol, fat, sugar and calories; stopping smoking and increasing exercise. We have to start promoting the idea that preventive medicine is something you do, not something you get.

By trying to prevent all diseases in all people we may limit some of the "joys" of living, but just being alive is a great pleasure. Our future is neither written in stone nor fixed irrevocably by genetics. "It's what we do hour by hour, day by day, that determines the state of our health;

whether we get sick, what we get sick with, and perhaps when we will die."[4]

Rules for Self-Health

This theme of "Feeling Good," a nationally televised weekly series on health, puts the responsibility for health where it should be, on the individual rather than on the physician. It also provides a reason for the practice of prevention in our daily lives and in our offices.[5] This, then, is the area of prevention where physicians can be the most help to themselves and to their patients. Our position of authority with patients and our community requires that we make an effort to live by what we recommend. To be credible we must provide an example in our own health behavior. The following health rules were originally designed for patient education[6] but as you read them over apply them to yourself. Would your patients see your own health habits as a motivating force or a laughing matter? Good habits are for doctors, too:

1. Pick a family doctor—a primary physician. Someone you can turn to when you are sick. He who cares for himself has a fool for a doctor.
2. Budget for your health care. Prepay it or put it aside but in 1974, a family will average over $600 for health related items.
3. Get your primary immunizations.
4. See your primary physician to establish a data base. Get all pertinent medical records transferred there. Work with him on a guardian maintenance program.
5. Don't demand a prescription every time you see the doctor. He may get tired of arguing and give in to you sometime. Nothing is often a good thing to do.
6. Know your own pertinent medical history, especially names, doses and side effects of all drugs (including over-the-counter) you are taking.
7. Wear a Medalert Tag for vital information (Diabetes, Epilepsy, dangerous drugs, allergies, Pacemaker, etc.).
8. Women—check your breasts once a month and have a Pap Smear once a year.
9. Men—keep your fingers crossed until a "Pap Smear" is invented that will do you some good.
10. Stop smoking.
11. Buckle your seatbelts.
12. Safety proof your home.
13. Stock and lock your medicine cabinet.
14. Diet. You don't have to clean your plate. Don't skip meals. Under-nutrition is a problem for teenagers, but for the general population over-nutrition is a bigger problem. Decrease carbohydrates especially free sugars, decrease fatty foods especially saturated (animal) fats.
15. Reduce to Ideal Body Weight. Life Insurance companies figure a year off your life for every ten pounds of extra body weight. There might be something you want to do with those years.
16. Exercise regularly. At least three times a week to maintain fitness. Almost every other day to increase fitness. See your doctor before any marked increase in activity level. Running a marathon distance (24 miles) in less than four hours will absolutely protect against a coronary for six years. Running even ten kilometers at an eight minute pace will protect you for two years. Now that's real preventive medicine. Swimming and biking are also good, but running is the most efficient—most exercise per unit of time. Even walking helps if you can maintain an army pace, four miles per hour. Endurance, not sprinting, is the aim. Lift ten pounds ten times rather than 100 pounds once.
17. Learn to relax. A playtime is important for children of all ages. Take regular vacations and be sure to schedule some time away from the kids.
18. If drugs (alcohol, tranquilizers, sedatives, stimulants) are a part of your usual day, cut it out. One out of ten people who are regular users will end up as chemically dependent. A drink is important when you get home from work, and a coming home ceremony is also important, but neither the drink nor the ceremony need be alcoholic. Caffeine and nicotine are also drugs.

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Annual Meeting

A Meeting this great can only happen once a year!

Rural Physician Associates

An Information Service for Rural Physician Associate Program Students

GERTRUDE FOREMAN,* L. YVONNE WULFF,* and JOHN E. VERBY, M.D.†

A cooperative project of the University of Minnesota's Rural Physician Associate Program and Bio-Medical Library provides senior medical students studying in rural communities access to medical literature. Student response to the MEDLINE and photoduplication service is favorable.

In a perceptive explanation of information service to rural health professionals, Bruce postulates that one variable in the low physician population ratios in rural communities may be the lack of access to necessary scientific and medical information.[1] This at a time when the "information explosion" is difficult for all medical practitioners to manage. Both the uneven distribution of health care personnel and the "information explosion" are well documented in the literature.[2-11]

There is a tendency for the professional population to concentrate where information is readily available through effective communication, i.e., where information can be obtained quickly and at minimum cost. If the city is recognized as a place where the maximum lines of communication converge, the invisible city, as conceptualized by Bruce, is a large, formally "organized community of individuals who share the same general interest and are able to interact with each other over large distances."[12] The invisible city of health care professionals is not clustered in a single geographic area.

Communication Channels

Although spatially separated, the population of this invisible city also depends upon communication channels which provide effective access to scientific and medical information, including the biomedical literature. The medical student educated in a metropolitan university learns the information seeking patterns exhibited by members of the profession working in an information rich urban environment. When rural practice is the goal, the medical student may feel disenfranchised unless additional patterns are introduced which allow full participation in the invisible city.

Start of Information Program

Senior medical students enrolled in the University of Minnesota Medical School's Rural Physician Associate Program enjoy the opportunity of experiencing medical practice in the rural community, but are separated from familiar educational library services. In the fall of 1974, the Rural Physician Associate Program and the Bio-Medical Library initiated an information program designed to supplement community library resources and to establish during student years those patterns for information seeking which would be applicable in rural practice (for the student and practitioner).

The Rural Physician Associate Program

"As a step toward relieving the shortage of physicians in small towns," the Rural Physician Associate Program was implemented in 1972.[13] The senior medical students participating in the program spend one year under the direct guidance of a community physician. According to Ciriacy, "the program provides the student with the opportunity to see and experience life as a physician in a nonurban setting and clarifies for him a physician's place in society, his social and civic obligations, and his responsibilities to patients . . . The student contributes to the care of a population of patients in a community while learning the principles of primary health care delivery."[14] In addition, the student becomes acquainted with treatment of common complaints often seen in the physician's office and has the opportunity of becoming sensitized to family patterning and dynamics. The student also develops an awareness of the role and responsibilities of other health professionals, experiences the importance of developing workable interprofessional relations, confronts medical-legal problems, and gains knowledge in consultation and referral.

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†Professor, Rural Physician Associates Program, University of Minnesota.

Bio-Medical Library Information Program

In the fall of 1974, following an evaluation of the first class of RPAP students at the end of their fourth year, representatives from the RPAP and the Bio-Medical Library concluded that the 38 students registered in the Rural Physician Associate Program required special information services. While a local hospital library can offer access to the world's biomedical literature, not all Minnesota hospitals have libraries.[15] Where local libraries were available, students would be encouraged to use them as a first source, an effort to acquaint them with one more of "the roles of the various allied health personnel and services" —that of the hospital librarian. In addition, students should have direct access to Bio-Medical Library to improve delivery time of materials and bibliographic services not locally available. Preceptors also were invited to use the information service program.

Goal of the Program

The goal of the program is to demonstrate to the medical students one communication channel which provides an access point to the biomedical literature. Establishment of the program fulfills three more specific objectives: (1) to provide information needed by students for patient care, study, research and decision-making and planning; (2) to acquaint students with an information seeking method which will be applicable to rural medical practice and (3) to introduce students to the role of the librarian in the health care delivery field.

The information program is based on existing Bio-Medical Library collections and staff with the primary service elements, the computer-produced bibliography and photoduplication, financed by the Rural Physician's Associate Program. The bibliography/medical article combination was selected as a viable means for the rural physician's access to information.

Computer Search Services

Computer-based bibliographic search services, such as MEDLARS (Medical Literature Analysis and Retrieval System), long have been familiar to some health professionals,[16] but it was not until the on-line, decentralized system, MEDLINE, (MEDLARS ON-LINE),[17] became operational that its use became widespread. With the larger Minnesota institutions already members of the MEDLINE system, smaller community hospital libraries and Area Health Education Centers may become members through the shared services concept.[18-19] With the information seeking skills learned during student years, the rural practitioner can make full use of the service provided. In a study of Astronomy students and faculty, Borman and Mittman found that students accept on-line bibliographic services more readily than do faculty and will incorporate the new capability into normal behavior patterns.[20]

MEDLINE

The MEDLINE bibliography provides references to journal articles.[21] According to Jones, "medical journals have . . . as their first function the role of being the archives of our knowledge to which . . . all subsequent investigators must turn." The student using "contemporary journals to report at the next session . . . Will have had one more experience which facilitates his utilization of the resources . . . and helps him acquire a habit which can service him well in later life.[22] A study conducted at Stanford University revealed that medical student periodical use reaches a peak in the fourth year.[23] Although the physical form of the periodical may change, the medical article undoubtedly will retain its significance as a means of communication.

Early Results of the Program

The information program has been operational for a short time, but the students apparently have found the bibliographies and journal articles a useful addition to their other resources for information. From September 15 to December 15, 81 requests were received by the Bio-Medical Library Staff. Of these 81, 7 were initiated by preceptors and 74 by students, with 24 students requesting services at least once.

During orientation week, a librarian spoke briefly to the students and descriptive material and request forms were given to each student. The explanatory material also was sent to the preceptors and the local hospital library. Three options are available: (1) bibliography only, (2) photocopy of journal articles only or (3) bibliography and selection of relevant articles by the librarian. Seven requests were received for the bibliography only, while 58 requests stated that selection of articles by the librarian plus the bibliography was needed. The 14 requests for photocopy only were for articles cited in the bibliography or were on subjects for which a bibliographic search had been done.

The subject requests cover a wide range of interests and often reflect goals of the Rural Physician Associate Program. That the student becomes acquainted with the treatment of common complaints often seen in a family physician's office is reflected in requests for information on breast feeding, diabetes therapy, and management of obesity. "The effects of environment and air pollution on mucosa of the nose and nasopharynx" implies an awareness of community conditions. That students learn to evaluate patients within the context of the family unit is indicated by "comparison of vasectomy and tubal ligation" or "non-compliance with therapy." Recognition of medical-legal problems is suggested by a request for "incidence of thrombophlebitis with intravenous therapy." "Surgical vs. medical treatment of lumbar disc disease" reveals student participation in decision making or, perhaps, the referral process. A preceptor's concern for community-wide preventive medicine is reflected in an information request on "mass screening with pap tests."

Mailing Problems

A complete account of the library service can be given only after evaluation from the students; however, several problems have been recognized by the librarians. A major difficulty involves the time needed to deliver the photocopied articles. Usually a computer search takes less than 15 minutes and articles can be selected and mailed within 24 hours, but mailing time is slow, both for requests coming to Bio-Medical Library and materials sent to the student. Although the requests are exceptionally well defined, on several occasions follow-up telephone calls would have been helpful for the librarian. More local hospital library development and subsequent use will help eliminate some of the time lag, as could use of the telephone. The information program can be modified after student feedback identifies other areas of concern.

Conclusions

While students in the Rural Physician Associate Program are experiencing life as a physician in the nonurban setting, they also are learning information seeking patterns useful in rural practice. Response to the library information program suggests that students are receptive of the computer-produced bibliography, with the majority requesting that the librarian select and send articles with the bibliography. Although spatially separated from familiar information sources, the prospective rural practitioners become citizens of the invisible city of health professionals through access to the biomedical literature.

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20-23. Will be found on page 190.

Public Health Nursing

Adult/Geriatric Nurse Practitioners in Minnesota

EVA ANDERSON VRASPIR, R.N., M.S.; ELAINE COOLEY, R.N., M.S.
and GEORGE WILLIAMS, M.D.

Reporting data collected on the graduates of the Adult/Geriatric Nurse Practitioner Certificate Program from the University of Minnesota. Covers description of graduates; employment areas and settings; clients served; and problems encountered.

THE UNIVERSITY OF MINNESOTA, School of Public Health, Public Health Nursing Program has three educational programs that prepare registered nurses to function as "nurse practitioners." The first program, developed in 1971, is a nine-month post-baccalaureate Pediatric Nurse Associate Program. A second program was developed in the existing Master's degree course and offers either a pediatric or adult practitioner track. In 1972, a five-month continuing education program was developed to prepare practicing registered nurses to function as Adult/Geriatric Nurse Practitioners This is offered in Minnesota communities where there is interest and need. This paper focuses on the continuing education Adult/Geriatric Nurse Practitioner Certificate program.

Nurse practitioners prepared in this program function as colleagues of the physician in delivering primary health care to individuals and families.* While they are assuming some tasks and responsibilities formerly associated with physician practice only, they are prepared to function interdependently on the health care team with the physician, social worker and other health professionals. The nurses' role focuses primarily on care of the well adult, care of patients with minor acute health problems, and care of the stabilized chronically ill patient.

The expanded role involves increased nursing accountability with significant primary care responsibilities which are shared with the physician. These responsibilities would include patient health assessment through history taking and physical examination; patient medical management through collaboration with a physician or direct referral; and, patient education and counseling with special concern for the psychosocial elements of health and disease.

In 1972-73, data from the evaluation of the pilot project was reported in MINNESOTA MEDICINE, Supplement, October 1973 and indicated selected R.N.s can deliver primary health care and that an educational program to prepare Adult/Geriatric nurse practitioners could be taught effectively away from the University. Since that time programs have been conducted in the Metropolitan area, St. Cloud, Grand Rapids, and Wadena.

Six programs have been completed between June 1, 1972 and December 1974. Sixty-eight nurses applied for admission, 55 were accepted and 52 satisfactorily completed the five-month course of study. The sites of the six programs were Thief River Falls and the areas mentioned above. Table 1 shows the class sizes and locations.

TABLE 1
Program Sites and No. of Graduates
December, 1974

Sites	No. Applied	No. Accepted	No. Graduated
Thief River Falls	3	3	3
St. Cloud	17	15	14
Grand Rapids	12	10	10
Wadena	13	8	7
Metro area (2 programs)	23	19	18
Total	68	55	52*

Attrition Rate = 5.5%
*Two male nurses applied, two were accepted and one graduated. Included in the above figures.

Two programs were in session in 1975, one in Mankato and the second in the metropolitan area. Sixty-four nurses applied for these programs; 23 were accepted. In addition 47 applications from nurses around the state are currently on file.

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*Primary Care is defined by the U.S. Public Health Service as: (1) Entry point into a health care system; (2) Range of services adequate for meeting the great majority of daily personal health needs which include maintenance, evaluation and management of symptoms and appropriate referrals.

A composite description of a typical graduate of the program is a nurse, age 36, with 10-years experience, married with two children and a graduate of a diploma program in nursing. Table 2 shows age and experience ranges and a breakdown of basic nursing preparation.

TABLE 2
Basic Nursing Preparation Age and Years of Experience in Nursing of Graduates
December, 1974

Basic educational preparation in nursing	(No. of Graduates)				
	Associate Degree	Diploma	B.S.	M.S.	Total
	1	39	10	2	52
Age of graduates	Range: 24-62 years of age Median age: 36.5 years Mean age: 37.3 years				
Years of experience in nursing	Range: 2-38 years experience Median: 10 years experience Mean: 12.3 years experience				

Current employment data of the nurse practitioners are shown in Tables 3 and 4. Forty-three of the 52 graduates are employed full-time, six part-time, and three unemployed. All graduates of this program are salaried. Salary range is $8000 to over $15,000 with the median salary $12,000. None are practicing independently.

Areas of practice are shown in Table 3. Hospitals, public health nursing agencies and private physicians are the predominant employment sites.

TABLE 3
Employing Sites of Nurse Practitioners
December, 1974

Agency	No. of Nurse Practitioners
College Health Service	1
Senior Citizen High Rise	3
Hospital—Acute Care	
In-patient service	8
Out-patient service	7
Indian Health Service	1
Industrial Setting	1
Nursing School Faculty	1
Nursing Home	4
Physician's office or clinic	8
Public Health Nursing	8
State Hospital System	3
Veterans' Administration System	4
Unemployed	3
Total	52

There is a lack of primary care providers in rural areas of Minnesota.[1-3] One of the program objectives was to prepare nurse practitioners in and for the rural communities in Minnesota. Sixty-eight percent of the graduates of the program practice in rural and outstate urban areas; 32% of the graduates practice in the metropolitan area. Table 4 shows the counties and communities in Minnesota where nurse practitioners are located.

TABLE 4
Counties and Communities in Minnesota Where Nurse Practitioners Are Located
December, 1974

County	Community	No. of Nurse Practitioners
Aitkin	Aitkin	2
Benton	Foley	1
Cass	Pine River	1
Crow Wing	Brainerd	3
Hennepin	Minneapolis	9
	Minnetonka	1
Hubbard	Park Rapids	1
Itasca	Mahnomen	1
Mille Lacs	Onamia	1
Morrison	Little Falls	1
Otter Tail	Parkers Prairie	1
Pennington	Thief River Falls	2
Ramsey	St. Paul	6
Stearns	St. Cloud	7
Todd	Bertha	1
	Long Prairie	1
Wadena	Menahga	1
Wright	Monticello	1
	Waverly/Cokato	1
Out of State	Colorado	1
	Wisconsin	1
Total		52

The educational program focuses on providing care to adults including geriatric patients. The graduates of the program spend 67.4% of their time delivering care to the adult and geriatric segment of the population. Nine percent of their time is spent in delivering care to children. Those few nurses involved in care of children have received additional on-the-job preparation from the physicians with whom they are associated. The

TABLE 5
Percentage of Time Spent by Nurse Practitioner With Clientele Groups
December, 1974

Clientele Groups	% of Time (averaged)
Senior Citizens—over 65	49.0
Middle-aged adults—35-65	8.4
Young adults—20-35	9.6
Adolescents—13-19	5.1
Children—0-12	9.0
Family groups	5.0
Group education	1.5
Students (nurse as teacher)	6.6
Community organizations	1.3
Inservice education	4.5
Total	100.0

employing agencies' policies and the needs of the clientele they serve dictate the kind of services provided. Nurse practitioners spend 81% of their time delivering direct patient care to various age groups and in other activities.

Nurse practitioners are utilized and function in a variety of settings. All of the nurse practitioner graduates of the School of Public Health's Adult/Geriatric Nurse Practitioner Certificate program function in collaboration with a physician or group of physicians. The nurse may be the only professional delivering care at a particular site, but she has physician consultation readily available. The nurse practitioner as an independent care giver performs health assessment and initiates primary care in ambulatory clinics, physician's offices, and employee sick clinics. In addition nurse practitioners perform screening activities for early detection of disease in well women's clinics, high-rise buildings for the elderly and early periodic screening of children.

In other settings, again dependent upon consumer and agency needs, nurse practitioners compile initial and interval histories, perform physical examinations, pre-natal exams and care, and post-operative follow-up care. They order diagnostic tests, regulate diets and medications under pre-established protocols, initiate treatment on selected minor acute illnesses, and follow stabilized chronically ill patients. Home visits are made as needed, as well as hospital and nursing home rounds on selected patients. Nurse practitioners assume an active role in patient teaching and counseling in areas of identified health problems as well as in prevention of illness and promotion of health. The nurse consults with or refers to the physician as the patient's condition indicates.

In a study now going on, selected nurse practitioners will be asked to log all their activities including assessment, problem solving, decision making and action for each of their patients.

This is a new role for the nurse. Assuming this new role involves change in thought, action and attitude of not only the nurse, but the physician, other nurses and all health professionals concerned with patient care. Other problems, difficulties and barriers to full implementation of the new role by the nurse practitioner are listed alphabetically:

1. Apathy on part of administration of employing agency.
2. Infringement on public health nursing role.
3. Lack of communication on treatment or follow-up of referred patients, particularly in neighborhood clinics and senior citizen high-rise clinics.
4. Lack of understanding by physicians of the role of the nurse practitioner.
5. No release from previous responsibilities and administrative duties, particularly true in nursing homes.
6. No third party payment available for services provided by nurse practitioners in any setting.
7. Personal insecurity of nurse practitioner in assuming role responsibilities.

One interesting finding is that consumer response has not been a problem in role implementation.

Summary

Since June, 1972 the nursing program in the School of Public Health, University of Minnesota has conducted a continuing education program to prepare Adult/Geriatric nurse practitioners. Data collected on the 52 nurse practitioner graduates indicate that 47 are practicing in sixteen different Minnesota counties in ambulatory, acute and long term care facilities. Nurse practitioners spend most of their time caring for adults (49% on senior citizens) and 81% of their time delivering direct patient care.

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CME '76

May 20-21, 1976

Rochester, Minnesota

In Memoriam

A. C. Davis, M.D.

Dr. Austin C. Davis, retired Mayo Clinic internist, died November 5. He had been on the staff of the Clinic for 31 years before his retirement.

Born in Libertyville, Iowa, in 1891, he received the degree of bachelor of arts in 1913 and that of doctor of medicine in 1916 from the State University of Iowa. He came to Rochester in 1923. Dr. Davis did much original work on the thyroid gland and the pituitary and suprarenal glands problems.

He was certified as a specialist in internal medicine by the American Board of Internal Medicine; a fellow of the American College of Physicians and a member of the American Medical Association, the Central Society for Clinical Research, the Alumni Association of the Mayo Foundation, the Minnesota Society of Internal Medicine and the Zumbro Valley Medical Society. He was an Associate and 50 Club Member of the Minnesota State Medical Association, and a former secretary-treasurer of the Southern Minnesota Medical Association.

Carl A. Traeger, M.D.

A native of Bloomington, Illinois, and a graduate of Bradley University and the University of Minnesota School of Medicine, Dr. Carl A. Traeger, 86, Faribault physician, died November 26. He had practiced medicine in Faribault for more than 48 years.

Dr. Traeger was the recipient of the cherished Selective Service Medal and Certificate of Merit, presented by Congress to him, for his, service as a member of the Selective Service Board during World War II. He was a member of the American Medical Association and the Rice County Medical Society, and a Life and 50 Club Member of the Minnesota State Medical Association.

Dr. Traeger is survived by his wife, Ruth.

William G. Atmore, M.D.

Dr. William G. Atmore, 52, orthopedist at the Duluth Clinic, died November 22, while hunting near Grand Rapids. He was a graduate of the University of Minnesota Medical School.

Dr. Atmore was certified by the American Board of Orthopedic Surgery and elected a fellow in 1962. In addition he was a founding member of the American Orthopedic Foot Society and was current Vice President of the Minnesota Orthopedic Association, Assistant Clinical Professor of Medicine at the University of Minnesota Duluth Medical School, an officer of the Minnesota-Dakotas-Manitoba Orthopedic Society, member of the American Medical Association, the Minnesota State Medical Association and the St. Louis County Medical Society.

His wife, Peggy; two daughters, Mary and Kathleen; and four sons, Mark, Michael, Thomas and William Jr. survive him.

Gershom J. Thompson, M.D.

Dr. Gershom Thompson, Sr., retired Mayo Clinic urologist, died November 2 after a lengthy illness. He had retired from the Clinic nearly ten years ago after 35 years of service. Dr. Thompson was a physician for Lyndon Johnson when he was vice president.

He was a member of the Zumbro Valley Medical Society and the American Medical Association, and an Associate and 50 Club Member of the Minnesota State Medical Association.

He is survived by his wife, Maxine, and a son and daughter.

Jack Tullus Murphy, M.D.

Dr. Jack Murphy, 58, St. Paul physician, died November 1. A graduate of Northwestern University Medical School, Dr. Murphy completed his post-graduate work at the Mayo Clinic in Rochester.

He was a Fellow of Internal Medicine, Mayo Clinic, Medical Director of the St. Paul Insurance Companies, member of the Staff of St. Joseph's Hospital, and a member of the American Medical Association, the Minnesota State Medical Association and the Ramsey County Medical Society.

Dr. Murphy is survived by his wife, Virginia, and three sons, William, Jon and Dennis.

Phillip A. Rierson, M.D.

Dr. Phillip Rierson, Minneapolis pediatrician, died September 9. He was a graduate of the University of Minnesota Medical School.

Dr. Rierson was a member of the American Medical Association, the Minnesota State Medical Association, and the Hennepin County Medical Society.

His wife, Carol; two sons, Eric and Seth; and a daughter, Gretchen, survive him.

Richard K. Runquist, M.D.

Dr. Richard Runquist, 45, Cambridge physician, died August 28. He was born in Cokato and practiced medicine in Anoka, Cambridge and Pine City.

Dr. Runquist was a member of the American Medical Association, the Minnesota State Medical Association, and the East Central Minnesota Medical Society.

His wife, Carlyn; two sons, Keith and Stephen; and a daughter, Linda, survive him.

F. C. Meyer, M.D.

Dr. Frederick C. Meyer, Kenyon physician for nearly 44 years, died October 2 at the age of 71. His Model-T Ford was a familiar sight on house calls in Kenyon at a time when medical care was perhaps less scientifically advanced than it is today.

He was a charter member of the Kenyon Lions Club and a member of the Academy of Family Physicians, American Medical Association, and the Rice County Medical Society, and a Life Member of the Minnesota State Medical Association.

Dr. Meyer is survived by his wife, Icle, two sons, Dr. Rodney Meyer of Brainerd and Dr. Russell Meyer of Moorhead; and two daughters, Dr. Barbara Puumala of Cloquet and Nancy of Bloomfield, Nebraska.

James C. Masson, M.D.

Dr. James C. Masson, last surviving surgeon to train under Drs. William J. and Charles Mayo, died December 7, at his home in Rochester. He was 94 years of age.

Dr. Masson retired in 1949 from the Mayo Clinic after 34 years on the staff, and with him, retired the title chief surgeon of the Clinic, a title held by only a handful of famed Mayo surgeons. He was born in Owen Sound, Ontario, Canada, and earned his medical degree from the University of Toronto Medical School.

He was active in a score of state, national and international surgical societies and associations and was a past president of the Minnesota Society of Obstetrics and Gynecology.

Dr. Masson is survived by his wife, Ruth; two sons, Dr. James Masson of Rochester, and Stanley of Winter Park, Florida; and a daughter, Louise.

Book Reviews

SISTER KENNY—THE WOMAN WHO CHALLENGED THE DOCTORS. By Victor Cohn. Univ. Minn. Press 1975. pp 302. $16.50.

Sister Kenny had no formal training in nursing. This fact is fundamental to the assessment of her contribution in polio therapy. She was not taught a web of misinformation from which she would need to disentangle herself before she could proceed to learn from nature. It was as easy for her to appreciate the fallacies of immobilizing paralyzed limbs and torsos as it was impossible for members of the learned professions to discard what they had been taught.

Her assertions to physicians that their therapy was disastrous and she (alone) could remedy their mistakes were ludicrous to them. How could this bush nurse from the outback of Australia teach real M.D.s anything? Such chutzpah. Victor Cohn tells the absorbing story of her Cinderella career with sympathy, knowledge, and conclusions that I think are correct. Ms. Kenny made enormous contributions not only to the therapy of paralyzed polio victims but also to the whole field of physiotherapy. She is certainly the inspiration of thousands of therapists if not of their mentors, the physiatrists themselves.

It was inevitable that the recognition she so desperately sought, the approval of the entire medical profession, in her lifetime would be denied her. Her claims of cure, her contempt of authority, her cultist approach alienated the Establishment. Hoi polloi thought otherwise and in this country she stood first in polls of popularity—a female David who slew the Goliath.

Victor Cohn has caught the spirit of this woman. The book reads like a novel that cannot be laid aside (and kept this reviewer up the most of one night). The need for therapy of masses of paralyzed children is probably past. But there are lessons for us physicians to learn from her unique career. Cohn describes in merciless detail the debacle of the Kenny Foundation so nearly ruined by Kline, Fadell, and the Koolishes. This chapter should be read by every philanthropic board member. There are booby traps prepared for these honored but possibly unwary men. I recommend Cohn's Kenny to the public for interesting reading and to the profession for a bit of breast beating.

Reuben Berman, M.D.
Editor Emeritus

AWAKENINGS, by Dr. Oliver W. Sacks, Doubleday & Co., Inc., Garden City, New York, 1974, 249 pages. Price: $7.95.

This is an account of a clinical experience with post-encephalitic Parkinsonian patients. His case reports and his understanding illustrate a number of points:

1. Epidemic encephalitis lethargica has been seen in epidemics prior to the last one of 1918-1926, and may make another appearance.
2. The description of some of the transient manifestations of acute encephalitis lethargica remind us of the activities of victims who were subjected to the rites of exorcism. Are there indeed sporadic cases of encephalitis lethargica in the absence of epidemics? Or are the victims of exorcism patients with another type of encephalitis?
3. Efficient hospital management, although economical in time and money, may not always be in the best interest of the patient.
4. Treatment with levodopa is beset by episodes of hyperactivity, physically as well as mentally, and sometimes followed by severe setbacks. Dr. Sacks concludes that purely mechanistic-biochemical viewpoints fail to comprehend the nature of the disease and the reaction to levodopa. In spite of his extensive citations of Donne, Leibnitz and Freud, one gains the impression that Dr. Sacks is aware of the possibility that we are dealing with a more complex biochemical abnormality, only part of which is influenced by levodopa, and that further biochemical information might lead to more satisfactory therapeutic approaches.

The book is an interesting and moving account of the disease and its present treatment. It points out many aspects of the disease and might awaken the interest of other biochemists, which in turn may possibly lead to happier awakenings.

Horace H. Zinneman, M.D.
Veterans Hospital

HANDBOOK OF LEGAL MEDICINE, A. Moritz, R. C. Morris, C. S. Hirsch. C. V. Mosby Co., St. Louis Feb. 1975. $10.25, 286 pages.

This is a fourth edition in soft cover, pocketbook format. The authors are a pathologist, a practicing lawyer, and a forensic pathologist. The 260 pages are equally devoted to a short review of forensic pathology and to legal problems in medicine. By necessity, this is a superficial review of these fields and its strength lies in the selected references. There are glaring inadequacies, like the omission of high velocity projectile injuries or the statement in chapter 28, that the performance of an abortion is a ground for license revocation. In the glossary, we find an explanation of "nucleus pulposus" but not of the doctrine of "res ipsa loquitur."

This small book may be intended for fledgling lawyers, rather than for physicians. It will be of very little help to the physician who needs to know more Legal Medicine.

H. W. Heupel, M.D.
Minneapolis, Minnesota

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STUDENT HEALTH SERVICE, Director, Mankato State University. Located in South Central Minnesota: on Campus enrollment of 10,000 students; metropolitan area of 50,000; current Minnesota license necessary. Salary competitive, five-day work week, liberal vacation, and fringe benefits. Contact Karen Delesha, Administrative Director, Student Health Service, Mankato State University, Mankato, Minnesota 56001, phone (507) 389-2726. Equal Opportunity/Affirmative Action Employer.

FAMILY PRACTITIONER needed to join other GP at the Pine City Clinic. New Clinic facilities including lab and x-ray. Excellent opportunity for rapid growth. Contact Oskar P. Friedlieb, M.D., 307 First Street North, Virginia, Minnesota 55792 or Ruel Martinson, M.D., Pine City Clinic, Pine City, Minnesota 55063.

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FAIRMONT—FAMILY PRACTICE OR INTERNIST—Opportunity with multi-specialty clinic. Over the past four years the Fairmont Medical Clinic has added four new physicians to its staff. At the present time we are pursuing one additional man for the spring or summer, 1976. New clinic adjacent to a new 114-bed hospital in a rapidly growing community. Starting salary open, with early incentive, liberal time-off allowance and fringe benefits. Contact D. E. Grandgenett, Fairmont Medical Clinic, P.A. 56031 (507) 238-4263.

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Index to Advertisers

Advertising Council 182, 184
Allied Medical Audit Control, Inc. 210
Anderson, C. F., Co. 184
Burroughs-Wellcome Co. 178
CARE 184
Classified Advertising 208
Cooper Laboratories, Inc.................... 193
Dahlberg Hearing Aids 176
Dow Pharmaceuticals 171, 172, 173, 174
Finley & Friday, Inc. 146
Kjell Bergh Borton Volvo, Inc. 150
Lilly, Eli, & Co. 156
Medical Protective Company 150
Metropolitan Medical Center Symposium 182
Options Company of Minneapolis 148
Pharmaceutical Mfrs. Assn. 194, 195
Roche Laboratories ....Cover 2, 145, Cover 3, Cover 4
Roerig and Company 153
Smith, Kline & French 154
Volvo, Kjell Bergh's Borton 150

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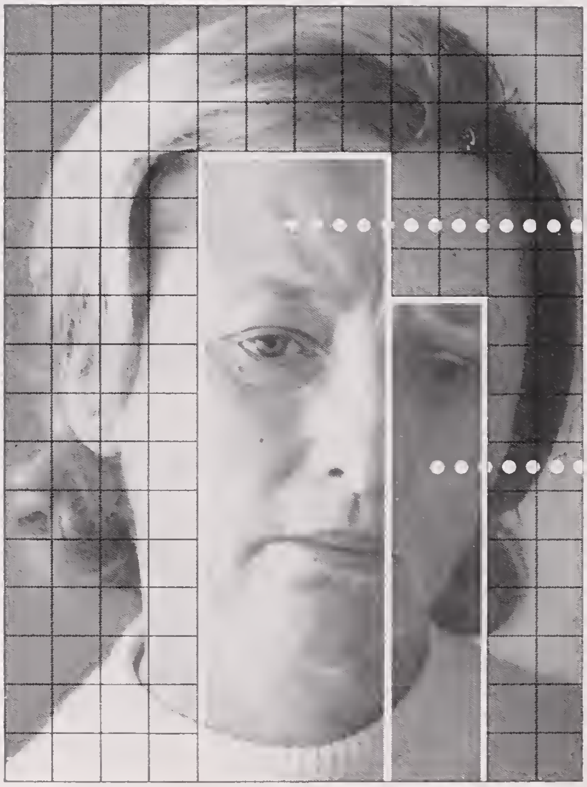
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with associated
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t possible hazard.
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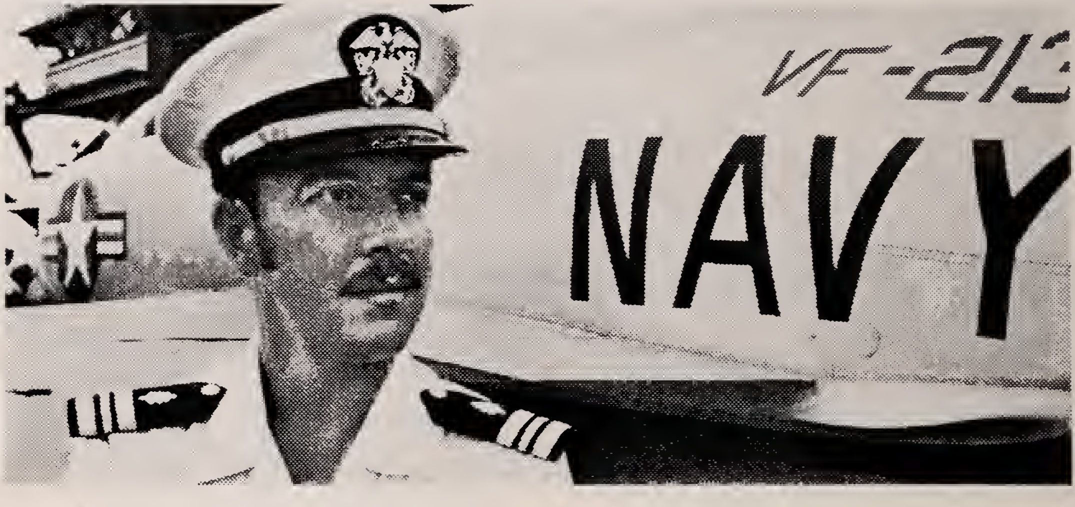

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President's Letter

Care with Caring

In the past several years the Health Planners, Bureaucrats and Politicians have developed phrases which are supposed to describe what physicians "do." For most people these have different meanings—or, as Humpty Dumpty in *Alice Through the Looking-Glass* scornfully said, "When *I* use a word it means just what I choose it to mean—neither more nor less." Ask the next 10 people you meet what they understand by the terms "Health Maintenance," or "Health Care Delivery," or try "Health Service Agency." What are your definitions?

The problem arises when such phrases find their way into law and then are defined, not by physicians, but by the politicians. We must then all accept or rebel against such definitions. Too often it is too easy or too late to do more than accept them.

What a doctor does is unique in that it involves others. These "others" are called patients. Actually they are human beings seeking help for what they perceive as something not right—or perhaps the fear of getting that way. How the doctor reacts to these people, what he does about their problems, and how they feel about the situation is what "caring" medicine is all about.

At the risk of adding yet another confusing phrase, I would like to announce that the Minnesota Academy of Family Physicians' motto this year is "Thirty Years of Care with Caring." Family Physicians have come to feel that their specialty in breadth—not limited by the patient's age, sex, organ system, or disease entity—uniquely trains them to see the patient in a "caring" manner. This emphasis on the patient as a personality who is a part of a family unit, rather than as a disease or abnormality, is not unique to Family Practice. Perhaps only the opportunity to develop it to such a great extent is more readily available in Family Practice.

Medical educators have come to feel that this "caring" attitude is an art which has developed with time in the past. In today's world the luxury of learning from years of practice is no longer acceptable. We must make an effort to teach the "Art of Caring" to the medical student and the young doctor in training.

Unfortunately this, too, sometimes comes out in jargon. We find our own Family Practice Residents being trained to "evaluate patients' total health needs," "assume responsibility for comprehensive and continuing health care," and "to act as a coordinator of health services." There must be constant vigilance lest the jingoism and jargon become substituted for the real meaning. The exposure of the young doctor to a role model of the caring physician currently seems to be the most effective teaching device.

As we develop better methods for teaching this art we will be on the threshold of a new era in medicine. "Care with Caring," universally taught and widely practiced by physicians in all specialties, for all patients, will ultimately be better than all the meaningless jargon ground out by the planners, politicians, and bureaucrats. Out of the heritage of medicine's past must come the direction for the future. We must not be swayed by ill-defined phrases. What the physician has always given and must continue to give to his patients is genuine "Care with Caring."

Jo E. Anderson M.D.

President
Minnesota Academy Family Physicians

Author's Note: I would like to thank Dr. Diessner for inviting the President of the Minnesota Academy of Family Physicians to share the President's Page for this issue of Minnesota Medicine. *MAFP appreciates and enjoys the continued close ties with MSMA.*

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Editor's Notebook

The Long Life in Minnesota

A month or so ago, I was browsing in a bookstore when a small book entitled "Yessir, I've Been Here a Long Time" caught my eye.[1] As I thumbed through its pages, reading about Americans who had lived to 100 years, I began to realize Minnesota had more than its share of the 31 centenarians interviewed for the book.

Here is a list of the book's hundred year citizens, their sex, and the states in which they live.

Age	Sex	State	Age	Sex	State	Age	Sex	State
109	F	Alabama	102	M	Mississippi	120	M	Georgia
105	F	New York	102	F	Georgia	101	M	Massachusetts
129	M	Florida	101	F	New Hampshire	100	F	Minnesota
103	F	Minnesota	104	F	New Hampshire	102	M	Massachusetts
104	F	Minnesota	103	F	Minnesota	104	F	Pennsylvania
102	F	Georgia	101	M	Mississippi	103	F	Minnesota
101	F	Ohio	103	M	Georgia	102	F	Massachusetts
100	M	Iowa	103	F	Wisconsin	102	F	Minnesota
100	F	Tennessee	104	M	Iowa	103	F	Wisconsin
108	F	Maine	101	F	New Hampshire	104	F	Wisconsin
						100	F	Minnesota

Six of the 31 centenarians, or 19 percent, come from Minnesota, and 11 of the 31, or 35 percent, are from the North Central States of Minnesota, Wisconsin, or Iowa.

This list does not contain all United States hundred-year-olds. After all, statisticians figure three of each 100,000 Americans will live to be one hundred, or about 6000 of every 200 million. Nor does the list prove we have more of these elderly citizens than any other state. Still, such a list serves as a starting point for writing about longevity in Minnesota.

Besides, the latest government vital statistics offer supporting evidence that Minnesotans live longer.[2]

Rank of State	Life Expectancy at Birth (years)		
	Male	Female	Both Sexes
1. Hawaii	71.0	76.8	73.6
2. Minnesota	69.4	76.8	73.0
3. Utah	69.5	76.6	72.9
4. North Dakota	69.2	77.0	72.8
5. Nebraska	68.9	76.6	72.6
6. Kansas	68.8	76.5	72.6
7. Iowa	68.8	76.5	72.6
8. Connecticut	69.0	75.9	72.5
9. Wisconsin	69.1	76.0	72.5
10. Oregon	68.4	76.2	72.1

For Minnesota these expectancy figures are impressive, and I suppose they have much to do with our hard work, good habits, and fine health care. But I would wager they also have a good deal to do with the homogeneous Nordic stock from whence we spring, the lack of a sizeable minority population, and our large rural population.

The latest United Nations' figures on life expectancy by country lend weight to the idea that Nordic peoples have long lives.[3]

Rank of Country		Life Expectancy at Birth (years)	
		Male	Female
1.	Sweden	72.0	77.4
2.	Norway	71.2	77.4
3.	Netherlands	70.8	76.8
4.	Iceland	70.7	76.3
5.	Denmark	70.7	75.9
6.	Japan	70.5	75.9
7.	Puerto Rico	68.9	76.0
8.	France	68.5	76.1
9.	Switzerland	69.2	75.0
10.	Australia	67.9	74.2

Living in rural regions, rather than cities, may also be important in achieving extreme longevity. Doctor Alexander Leaf, a physician at Massachusetts General Hospital, brought this to light in a *National Geographic* article three years ago.[4] Over a two year span, Doctor Leaf observed people in remote regions who commonly lived to 100 years. These regions were mountainous and removed from civilization. They included: an Andean village in Ecuador, the land of Hunza in Kashmir, and Abkhazian in Georgia of the Soviet Union. In these bastions of longevity, people live to be one hundred at three times the rate as in the United States.

Doctor Leaf found these peoples worked hard all their lives, constantly scampered up mountain trails, had long-lived parents, remained sexually active, enjoyed high social status, were happily married, had a strong sense of family continuity, enjoyed a sense of usefulness, and expected and looked forward to being one hundred.

Doctor Robert Samp, a physician on the University of Wisconsin faculty, attributes a long life to personality patterns and good living habits.[5] According to Samp, who has spent his professional life studying longevity, many old people share ". . . a lifetime history of middle-of-the-road moderation, serenity, interest in others and an interest in the future." Among the 25 factors that prolong life, he says these are important: (1) "Smoke within reason, keep drinking to social occasions and use it as a relaxant rather than a crutch; (2) "Sleep is essential for survival, and the older you get, the more you need"; (3) "Don't fight your enemies, outlive them"; and (4) "Seek reasons to be happy rather than counting the eternal damnations that beset you."

Incidentally, Minnesota physicians must follow this advice closely. I went over the obituary columns of *Minnesota Medicine* for 1975 and found this information:

Age at Death among Minnesota Physicians in 1975 in Years	Number of Physicians
30 to 40	1
40 to 50	4
50 to 60	8
60 to 70	8
70 to 80	11
80 to 90	10
90 to 100	7
over 100	2

What do I conclude from this random walk through the statistics and literature on aging?

To live to be one hundred: pick your parents, stay lean, keep moving, stop smoking, drink lightly, remain calm, chase girls (or boys), sleep well, ignore your enemies, climb mountains, don't retire, and if Ecuador, Kashmir, Soviet Georgia, Northern Europe, and Hawaii aren't your cups of tea, live in Minnesota.

Satchell Paige, that venerable baseball pitcher who remained in the major league into his sixties, had an even better set of rules.[6] These rules, he allowed, ". . . are mighty good for anybody":

Avoid fried foods which angry up the blood.

If your stomach disputes you, lie down and pacify it with cool thoughts.

Keep the juices flowing by jangling around gently as you move.

Go very light on the vices, such as carrying on in society—the social ramble ain't restful.

Avoid running at all times.

And don't look back. Something might be gaining on you.

Richard L Reece MD

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Contents—April, 1976

COVER PHOTOGRAPH—"Mrs. Bunyan's Son, Paul"
William T. Luckey, M.D. 278

PRESIDENT'S LETTER—Care with Caring
Jo E. Anderson, M.D., President, Minnesota Academy Family Physicians 215

EDITOR'S NOTEBOOK—The Long Life in Minnesota
Richard L. Reece, M.D., Editor-in-Chief 217

ORIGINAL CONTRIBUTIONS

Stroke: What's New? Cerebral Revascularization
J. I. Ausman, M.D. et al. 223

Urethritis Associated with Chlamydia
Lyle A. Weed, M.D. et al. 228

Disseminated Gonococcemia in Plasma Cell Myeloma
J. T. M. Bamford, M.D. and Steven L. Bloom, M.D. 230

Salt Load as a Trigger for Migraine
John B. Brainard, M.D. 232

EDITORIALS

Stroke: What's New?
Thoralf M. Sundt, Jr., M.D. 239

Hennepin County Doctor's Directory
John E. Smith, M.D. 241

Urethritis Associated with Chlamydia
Gordon W. Strom, M.D. 243

LETTERS TO THE EDITOR

Soviet Jewish Physicians
L. F. Cavazos, Ph.D. and Paul Reich, M.D. 243

Asbestos in Duluth Water
Arthur H. Wells, M.D. 244

MINNESOTA STATE MEDICAL ASSOCIATION—Annual Meeting
R. D. Semsch, M.D. and J. G. Mayne, M.D. 234

Nominees for State Offices 251

SPECIAL ARTICLE—Blinding Hockey Injuries
Richard C. Horns, M.D. 255

MINNESOTA DEPARTMENT OF HEALTH

Hepatitis-B Surface Antigen among Residents of An Institution for the Mentally Retarded
Heinz H. Bruhl, M.D. et al. 263

FAMILY PRACTICE

A Flexible and Functional Definition of Family Practice
Robert R. Thompson, M.D. and Charles G. Roland, M.D. 273

LABORATORY MEDICINE—The Child Who Fails to Thrive—Malabsorption
Ralph A. Franciosi, M.D. 277

GRAND ROUNDS—Asymmetric Septal Hypertrophy
Irl Don, M.D. 279

IN MEMORIAM 283

BOOK REVIEWS 270

CONTINUING MEDICAL EDUCATION 227, 245, 258, 278

CLASSIFIED ADVERTISEMENTS 246

INDEX TO ADVERTISERS 284

Volume 59, 4
Pages 211-284

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Stroke: What's New?

Cerebral Revascularization

J. I. AUSMAN, M.D., Ph.D.[†]; M. C. LEE, M.D.[*‡]; A. C. KLASSEN, M.D.[*‡];
E. L SELJESKOG, M.D, Ph.D.[†] and S. N. CHOU, M.D., Ph.D.[†]

By connecting the superficial temporal or occipital arteries to an intracranial cortical artery with the operating microscope, cerebral revascularization can be accomplished. This procedure may offer new hope in the prophylaxis and treatment of the stroke patient.

OVER 500,000 PEOPLE each year develop a stroke. Two hundred thousand of these die, while 75% of those surviving are partially or totally disabled. Stroke, or cerebral vascular disease, is the most costly disease in the United States in terms of death and disability. Cerebral arterial thrombosis is the cause of 70% of the strokes, while cerebral aneurysms, intracerebral hemorrhage and emboli account for the rest. The National Commission on Stroke has stated, "rehabilitation . . . is at best a poor . . . substitute for prevention. The highest priority objective must be prevention of this massive and catastrophic problem."[1] What then is being done to improve the situation?

Cerebral revascularization is a new procedure, much like coronary revascularization, by which additional blood can be brought to the brain by connecting vessels outside the skull to vessels on the surface of the brain. With cerebral revascularization, obstructive lesions in the cerebral blood vessels which are surgically inaccessible can be bypassed. Cerebral revascularization has been used in patients in the hope of eliminating transient ischemic attacks, of improving neurologic deficits after completed strokes, and of preventing subsequent strokes. A brief review of the background and basis for this new approach to cerebral vascular disease will be given.

This type of surgery on the blood vessels of the brain was not possible until the operating microscope was introduced into neurosurgery in the 1960's.[2] Generally the superficial temporal or occipital artery is dissected off the scalp and anastomosed to a cortical vessel which is greater than 1 mm in diameter (Figure 1). High magnification (10-20 power) and 10-0 suture material is required to make these anastomoses. Since Yasargil and Donaghy[3] performed the first cerebral revascularization procedure in 1967, over 500 have been performed throughout the world. The indications for the use of this new technique are not yet completely established; new applications and modifications are being considered and discovered continuously.

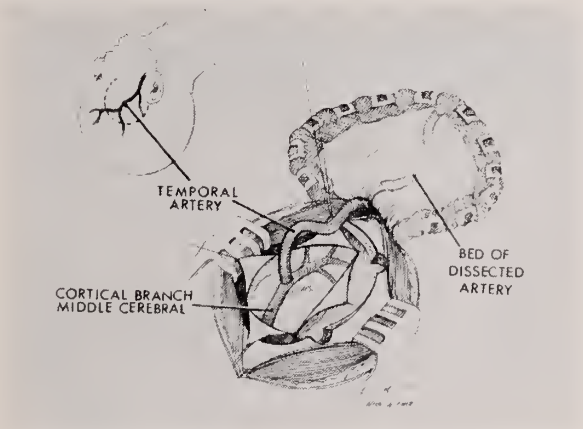

Figure 1—Drawing of incision (inset) for superficial temporal artery (STA) to middle cerebral artery (MCA) anastomosis.

From a review of the literature and from our own experience it appears that there are five categories of ischemic cerebral vascular disease

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[*] Supported in part by NINDS grant number NS-3364.

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See editorial, page 239.

in which cerebral revascularization can be applied (Table).

TABLE

1. TIA with surgically inaccessible lesions
2. Acute neurologic deficit from cerebral vascular occlusion
3. Fixed neurologic deficit post cerebral vascular occlusion
4. Compromised collateral circulation: Prophylactic revascularization
5. Dementia

TIA with a Surgically Inaccessible Lesion

Transient ischemic attacks (TIA's) are brief episodes of neurological dysfunction from which the patient recovers completely in less than 24 hours. Most TIA's are probably caused by emboli or compromised blood flow from stenotic lesions in major cerebral arteries. In a national study of cerebral angiography in patients with ischemic cerebral vascular disease including TIA's, obstructing lesions in the cerebral blood vessels, which are inaccessible to regular surgical approaches, were found in 40% of the patients.[4,5] These lesions occurred high in the carotid artery or commonly in the large vessels at the base of the brain.[5] With cerebral revascularization, such lesions can be bypassed and symptoms relieved.

Case Reports

Case 1

A 32-year-old woman had a sudden left hemiparesis from a right middle cerebral artery distribution infarction four years prior to admission. She made a good recovery, but one month before her admission she developed left hemisphere TIA's characterized by transient dysphasia and numbness of the right upper extremity. Angiography revealed a left middle cerebral artery stenosis (Figures 2a, 2b) and a right middle cerebral artery occlusion.

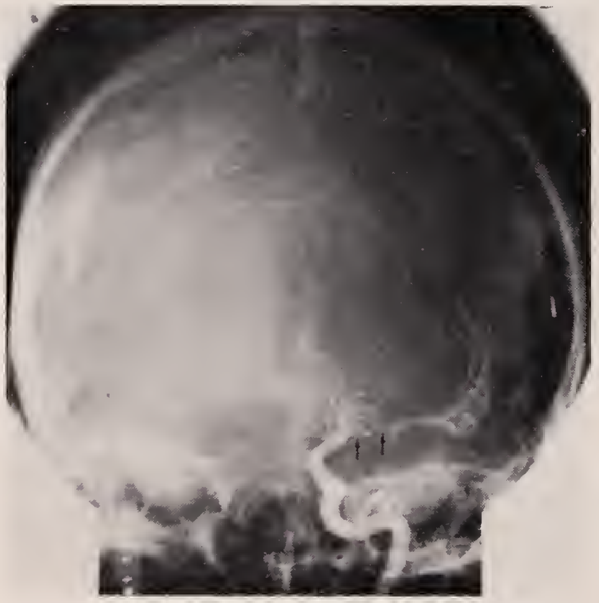

Figure 2a—AP L. carotid angiogram on Case 1 demonstrating stenosis of middle cerebral artery (arrows).

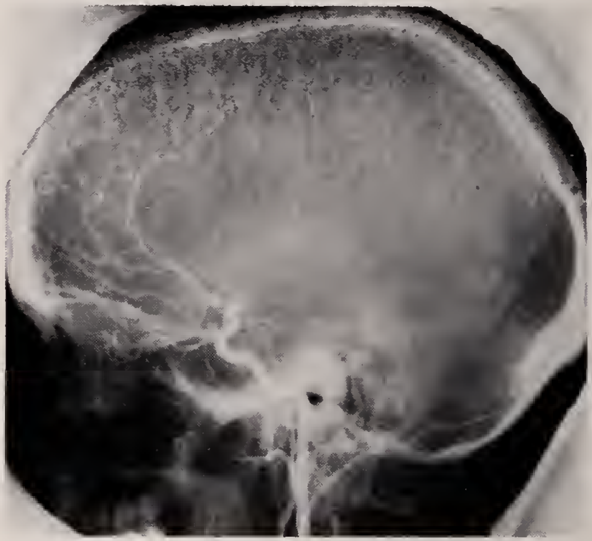

Figure 2b—Lateral left carotid angiogram on Case 1 with filling of only the anterior cerebral artery. Note absence of filling of middle cerebral artery distribution (pre-operative).

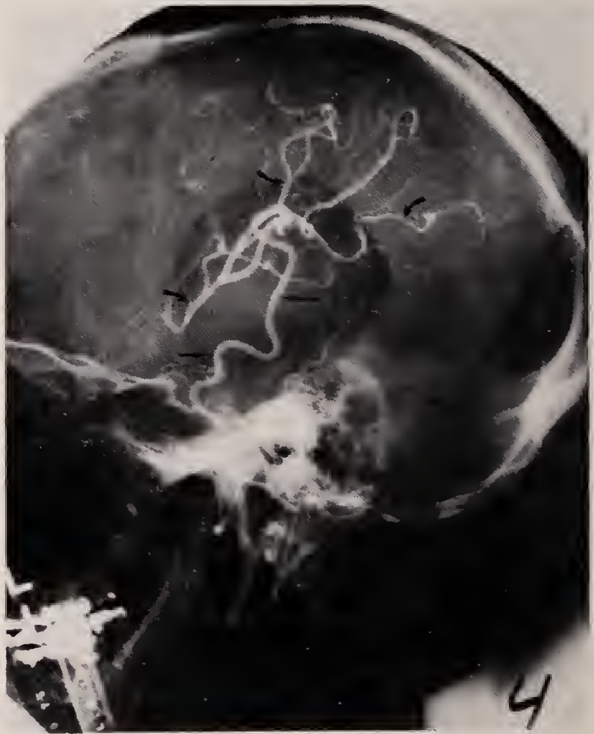

Figure 2c—Lateral left carotid angiogram on Case 1 demonstrating superficial temporal artery (straight arrows) filling middle cerebral artery distribution (curved arrows).

Anticoagulants did not alter her symptoms. Following a left superficial temporal artery (STA) to middle cerebral artery (MCA) anastomoses, she became asymptomatic. Good collateral flow to the brain through the anastomosis was demonstrated angiographically (Figure 2c).

Increased blood flow to ischemic cerebral tissue after such procedures has been reported[7] and the subsequent enlargement of bypass vessels confirms the presence of increased flow through these new channels.[8,9]

Acute Neurologic Deficit Immediately Following Cerebral Vascular Thrombosis

Crowell et al.[10] have reported that cerebral revascularization performed two hours after an acute cerebral vascular occlusion in dogs will decrease the size of the infarct and the clinical deficit. Similarly, monkeys with temporary middle cerebral artery occlusions which were released at varying times over an eight-hour period, had smaller clinical and pathologic deficits than those animals with permanent middle cerebral artery occlusions.[11] Other investigators have demonstrated a return in the oxygen availability to normal in the infarcted tissue of animals with revascularization. Revascularization is being instituted for the treatment of acute cerebral vascular thrombosis, in a few centers including the University of Minnesota. Carotid endarterectomy also is being attempted in patients within 24 hours of cerebral infarction.

Fixed Neurological Deficit from Cerebral Vascular Thrombosis

Several investigators[12,13,14] have reported clinical improvement after cerebral revascularization in 25-50% of patients with fixed neurological defects following cerebral infarctions. Although the pathology of cerebral infarction would imply that it would be un-rewarding to revascularize infarcted brains because of the obvious encephalomalacia, it is possible that ischemic neurons in the peri-infarcted tissue may be capable of functional recovery and that additional blood supply would enable further clinical improvement. This hypothesis has not been tested in animals and should be carefully evaluated in man. If it is true, it could significantly alter our concepts of the management of cerebral infarction.

Case 2

A 55-year-old man had a left cerebral hemisphere TIA and suddenly developed a right hemiplegia and dense dysphasia from a left internal carotid artery thrombosis. Six months after his infarction, a left STA-MCA anastomosis was performed, hopefully to improve his speech. Six months following surgery, a small improvement in his clinical status can be noted. Whether this improvement is related to surgery, rehabilitation therapy, or normal recovery cannot be determined.

More extensive application of the method in similar cases will be necessary to see if the procedure is of benefit in these patients.

Prevention of Future Infarction in Patients with Compromised Cerebral Circulation

About 3% of the population over 50 years of age has an asymptomatic carotid occlusion.[15] Ten percent of ischemic stroke patients have carotid occlusions; from data of the National Cooperative Study on Cerebral Vascular Disease, Lemak finds that some of these patients will develop subsequent strokes on the side of the occlusion.[16] It is thus possible that revascularization may prevent a second stroke in those patients with a previous carotid occlusion. No experimental or clinical evidence exists to indicate that such a procedure would be protective, although the approach seems reasonable.

Case 3

A 42-year-old woman had a right internal carotid artery occlusion four years before admission. She recovered from the left hemiparesis only to develop a right hemiparesis from a left internal carotid occlusion prior to admission. Her entire cerebral circulation was dependent upon her vertebral arteries and the collateral circulation to the cerebral hemispheres. The etiology of her occlusions could not be determined. A left STA-MCA anastomosis was performed after her neurologic recovery. A right cerebral revascularization was also done to provide this woman with sufficient additional collateral flow to protect her from future infarction.

Case 4

A 68-year-old retired male developed TIA's involving the left arm and leg four months prior to admission. Two months later he underwent an elective cholecystectomy and awoke with a left hemiplegia from which he recovered in weeks with a slight residual paresis. Another TIA involving the left arm and leg precipitated his admission. Examination revealed only a slight paresis on the left. Angiography demonstrated a right internal carotid artery occlusion. The patient has remained asymptomatic after a right STA-MCA anastomosis. Within five days of surgery the superficial temporal artery had doubled in size and was filling the right MCA distribution.

Case 5

A 52-year-old accountant developed the symptoms of vertebral-basilar insufficiency and a subsequent brain stem infarct. Angiography indicated only a right posterior communicating artery supplying the basilar artery and posterior fossa circulation. Both vertebral arteries were occluded. A further episode of brain stem ischemia occurred on anticoagulation. Cerebral revascularization was undertaken to provide additional collateral flow to the posterior fossa. An occipital artery to cerebellar artery anastomosis was performed. The patient has stopped anticoagulant therapy and there are no further symptoms. This is the first reported case of posterior fossa revascularization for vertebral-basilar ischemic disease.

Case 6

A 60-year-old male who had multiple episodes of left hemisphere TIA's for two years. Examination revealed only slight expressive dysphasia. Angiography demonstrated a left internal carotid artery occlusion and an ulcerated stenotic lesion at the right carotid bifurcation. The left hemisphere TIA's were attributed to compromised flow to the left hemisphere because of the left internal carotid occlusion and also the right carotid stenosis. Since the carotid artery must be temporarily occluded during an endarterectomy, the possibility of producing additional compromise in left hemisphere flow in this patient was avoided by performing a left STA-MCA anastomosis. The anastomosis was demonstrated by angiography to be patent and filling the left MCA distribution before the right carotid endarterectomy was performed. The patient is asymptomatic after both operations.

Dementia

Progressive dementia in adults may occasionally be due to occlusive cerebral vascular disease. Thus complete cerebral angiography may be indicated in the evaluation of dementia. Chater and Peerless[17] have reported the case of a 55 year old patient with dementia who was institutionalized and who had bilateral internal carotid and vertebral artery occlusions where angiography was performed. After bilateral STA-MCA anastomoses the patient recovered to assume work as a timekeeper. Post-operative angiography revealed excellent cerebral perfusion through both bypasses. Such improvement in dementia also has been reported in patients following carotid artery surgery.[18]

Discussion

Cerebral revascularization is a new procedure and its possible application in the treatment of ischemic cerebral vascular disease seems diverse. Greater experience is needed to determine the value of this approach to cerebral vascular disease. Cerebral revascularization is not a replacement for carotid endarterectomy, but is a procedure which can now be used for those patients with surgically inaccessible lesions in either the anterior or posterior circulation.

At the University of Minnesota, cerebral revascularization is being performed in most of the above categories. So far 25 revascularizations have been performed for TIA, cerebral vascular thrombosis, or prophylaxis Angiograms have been performed in 23 post-operatively and have shown patency in 91% of the anastomoses. Since the procedure only involves the dissection of a blood vessel on the scalp and a single blood vessel on the cerebral cortex, the patient has a remarkably benign postoperative course. All have been able to resume their normal activities on the day following surgery. The incidence of complications is very low. Mortality and significant morbidity generally have not been associated with this procedure.

All patients with the clinical diagnosis of stroke should be carefully evaluated to determine the etiology of their problem; in many instances this will require cerebral angiography. Angiography, to be helpful in the management of the stroke patient, should be of good quality and generally should include the four major blood vessels to the brain from the aortic arch and through the neck including the intracranial circulation and circle of Willis. With a knowledge of the entire vascular supply to the brain, a more informed understanding of the pathogenesis of the stroke and its management can be made. Cerebral revascularization may well be the most appropriate treatment for selected cases. Further evaluation of this promising method appears essential.

Summary

1. The background and technique of cerebral revascularization has been reviewed.
2. The clinical application in patients with: (a) transient ischemic attacks with an inaccessible lesion, (b) acute neurologic deficit from cerebral vascular thrombosis, (c) fixed neurologic deficit after cerebral vascular thrombosis, (d) anatomically compromised cerebral vascular circulation, and (e) dementia, have been evaluated.
3. The procedure has been established as having a low mortality and morbidity.
4. The need for its further evaluation is encour-

aged.

5. All patients with stroke should be thoroughly evaluated as soon as possible to determine the etiology of their problem; the most appropriate treatment for selected cases may well consist of cerebral revascularization.

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11:30-12:00 a.m.	Diagnosis of Acute Pancreatitis, Eugene P. DiMagno, M.D.
12:00- 1:30 p.m.	Luncheon at Campus Club, Coffman Union
1:30- 2:00 p.m.	Cystic Fibrosis, Warren Warwick, M.D.
2:00- 2:30 p.m.	Functioning Islet Cell Tumors, Laboratory Aspects, Edward Wong, M.D.
2:30- 3:00 p.m.	Sjogren's Syndrome, Laboratory Aspects, Gene G. Hunder, M.D.
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Urethritis Associated with Chlamydia

Clinical and Laboratory Diagnosis

LYLE A. WEED, M.D.[*]; THOMAS F. SMITH, Ph.D.[†];
GEORGE R. PETTERSEN, M.D., M.P.H.;[‡] and JOSEPH W. SEGURA, M.D.[#]

Chlamydia have been recognized as an important cause of urethritis in man. The biologic properties of the organisms and the clinical and laboratory diagnoses of these infections are reviewed.

IN THE VENEREAL DISEASE CLINIC at the Olmsted County Health Center (OCHC), about 70 to 80% of male patients (mostly 18 to 25 years of age) complaining of painful voiding and rather scanty, thin, mucopurulent discharge did not harbor *Neisseria gonorrhoeae,* as indicated by the results of the Gram stain and culture. Recently, several studies published on the subject of venereal disease have indicated that nonspecific urethritis accounts for 30 to 70% of the cases of urethritis[1-3] and, further, that *Chlamydia* are the causative agent in 20 to 50% of these infections.[4-8] Urethral specimens taken from patients seen at the OCHC have been examined for the presence of *Chlamydia.*[9] Of 501 of these specimens studied since October 1973, 116 (23.1%) have given positive results for *Chlamydia.* Because these patients have responded clinically to antimicrobial therapy, it seemed desirable to call to the attention of clinicians some useful facts about this group of organisms.

Biologic Properties

The microorganisms responsible for trachoma, inclusion conjunctivitis, lymphogranuloma venereum, and ornithosis are grouped together in the genus *Chlamydia.* Agents within this single genus, however, can be differentiated into two groups, according to whether or not the intranuclear inclusions produced in cell cultures stain with iodine (Table 1). Only ornithosis is caused by a subgroup B *Chlamydia.*

The term TRIC (trachoma-inclusion conjunctivitis) is appropriate for an organism obtained from the characteristic disease of the eye and producing typical iodine-staining inclusions in cell cultures. However, a similar isolate from the genital tract must be referred to by the genus name, *Chlamydia,* unless there is specific serologic evidence that it is the TRIC agent *(Chlamydia trachomatis),* the agent responsible for lymphogranuloma venereum, or another chlamydial agent.[10]

Chlamydia are similar in size to the rickettsiae, but unlike these organisms *Chlamydia* depend on the host cell for many essential metabolites. Furthermore, *Chlamydia* have never been cultivated extracellularly. On the other hand, at least one species of rickettsiae has been cultivated on a lifeless medium. Arthropods play a significant role in the transmission of many rickettsial species in nature but apparently do not function in this role in chlamydial infections.[11] Other pertinent properties of *Chlamydia* are listed in Table 2.

TABLE 1

Subgroups of Organisms in Genus Chlamydia

Subgroup	Organisms	Inclusion staining with iodine
A	Chlamydia trachomatis	Yes
B	Chlamydia psittaci	No

TABLE 2

Some Basic Properties of the Subgroup A Chlamydia

Obligate intracellular gram-negative bacteria
Inclusions formed in cell cultures detectable with iodine stain
Organisms transmitted by direct sexual contact
Sensitive to tetracycline therapy

---

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See editorial, page 243.

Clinical Aspects (Table 3)

In the male with chlamydial infection, there is usually some pain on voiding. This symptom may be mild or severe; it may have been of short duration before the patient sought help, or it may have been present continuously or intermittently for days or weeks. There is usually some exudate, especially when the patient arises in the morning. The exudate is likely to be thin, watery, or slightly purulent; occasionally, it is purulent enough to suggest gonorrhea. Even though the exudate appears watery, it will reveal pus cells when examined by Gram stain.

In the female the symptoms may be varying degrees of dysuria or vaginal discharge. Often there are no recognizable symptoms.

TABLE 3
Clinical Features and Treatment of Chlamydia Infections in Males

- **In urethra, infection gives rise to:**
  - **Scanty seropurulent exudate, with crusting of meatus and staining of underwear**
  - **Pain, which may be intermittent or continuous over a period of weeks**
- **Occasionally coexists with gonorrhea**
- **Treatment: tetracycline, 2 g/day for 10 to 14 days (0.5 g q.i.d.)**

Diagnosis

For diagnosis, certain considerations must be kept in mind. A history of pain on voiding or a scanty, thin exudate (or both) should suggest *Chlamydia* infection. However, if an exudate is present, this material should be tested by Gram stain and the urine sediment should be cultured for *N. gonorrhoeae*. For this purpose, the first 10 to 20 ml of urine are collected by the patient, and the cells are concentrated by centrifugation and plated onto a Thayer-Martin agar plate. The most productive specimen for the diagnosis of chlamydial infections is that obtained by a urethral swab (Calgiswab, Wilson Diagnostic, Glenwood, IL)[12] inserted 2 to 5 cm into the urethra or into the endocervix.[13]

Although urine or urine sediment is a useful source of specimens for the recovery of *N. gonorrhoeae* and T-strain *Mycoplasma, Chlamydia* can be recovered three to six times more frequently from urethral swabs.[14] The swab is extracted into transport solution (0.2 M sucrose in 0.02 M phosphate buffer, pH 7.2)[15] containing 50 μg/ml gentamicin and 25 μg/ml nystatin[6,9] and then transferred to the laboratory as quickly as possible. Aliquots of the specimen extract are then inoculated into McCoy cell cultures.[6] Identification of *Chlamydia* may be accomplished in two to six days.

Comment

Much research is needed to improve the techniques for isolation and for identification and classification of the various strains, and also to relate *Chlamydia* infections to other clinical conditions. Similarly, the role of *Chlamydia* and other organisms such as *N. gonorrhoeae,* T-strain *Mycoplasma, Trichomonas vaginalis, Candida albicans,* and herpes simplex virus acting individually and in concert in genitourinary tract infections should be investigated. The optimal treatment regimen of tetracycline therapy for *Chlamydia*-induced urethritis needs to be established.

The purpose of this preliminary report is to alert clinicians to the probable role of *Chlamydia* in certain genitourinary abnormalities that appear to respond well to treatment with tetracycline.

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Disseminated Gonococcemia in Plasma Cell Myeloma

JOEL T. M. BAMFORD, M.D.* and STEVEN L. BLOOM, M.D.*

Gonococcemia occurred in a patient with multiple myeloma, undergoing dilatation and curettage for dysfuntional uterine bleeding. A culture obtained from a four mm punch biopsy of a skin lesion confirmed the etiology most rapidly. Although it is well known that bacterial infections are common as serious complications of plasma cell myeloma, two recent reviews[2,7] give no specific references to Neisseria gonorrhea as a causative agent. This case is unusual because of a generalized distribution of a large number of tender hemorrhagic pustules resulting from a gonococcemia in a patient with previously undiagnosed plasma cell myeloma. A brief discussion of the pathogenesis of increased susceptibility to a bacterial infection in myeloma and the available diagnostic tests for a confirmation of gonococcal bacteremia are given.

Case Presentation

A FORTY-EIGHT-YEAR-OLD woman with a four-day history of increasing vaginal bleeding was admitted for possible dilatation and curettage. She had noted increasing dizziness over the two days previous to admission.

Past Medical History

No history of allergies or previous surgery. She had pneumonia two years ago. Denies past venereal disease. Gravida 7, para 6 with one spontaneous abortion 10 years ago. General health has been good, except for easy fatigability over the last two months.

Physical Examination

On admission there was pallor, weakness, vaginal bleeding and a dilated cervix. The blood pressure was 120/60. The pulse was 80 and regular. Respirations were normal. There were no skin lesions, lymphadenopathy or splenomegaly.

A Urinalysis and culture were negative. The white count was 10,500 with a sedimentation rate of 115 and a normochromic, normocytic anemia. The total protein of 11.2 gm% with an albumin of 4.0 gm% suggested multiple myeloma. A bone marrow demonstrated sheets of myeloma cells and a negative stain for iron. The urine was negative for Bence-Jones protein. A protein electrophoresis showed a total protein of 9.1 (normal, 6 to 8 grams %), albumin 3.65 (normal, 3.7 to 5.4), globulin alpha I 0.23 with normal 0.05 to 0.41, Alpha II 0.67 with normal 0.36 to 0.71, Beta 0.73 with a normal 0.04 to 0.95, Gamma 3.73 with normal 0.62 to 1.62. A complete blood profile was normal except for a BUN of 6 (normal, 10-20), and a SGOT of 80 (normal, 10-50).

Xrays including a barium enemia, skull, lumbar spine, pelvic, and chest were all negative. A VDRL was negative.

Hospital Course

During the initial two days of hospitalization she had several pelvic examinations. On the evening before the dilatation and curettage, she had a fever of 103 degrees. The following morning two hemorrhagic pustules on her hands were noticed. These were originally thought to be cigarette burns.

Following the surgery, the vaginal bleeding ceased. Over the next 12 hours about 10 hemorrhagic, tender pink lesions developed over the distal extremities. Over the following 12 hours about 200 similar pink lesions developed in a generalized pattern. These were all somewhat tender and palpable. With time some of these lesions became hemorrhagic pustules. Two of these hemorrhagic pustules, one on the palm and one on the sole, had lymphangitic spread proximally.

A gram stain of two pustules was negative. A gram stain of the cervix demonstrated many gram negative bacteria with a few extra-cellular gram negative diplococci. A gram stain from a crushed biopsy of a new lesion was negative for bacteria. Oral pharyngeal, rectal, cervical cultures were taken. While febrile six blood cultures were taken.

During the post-operative period the temperature rose to 103 degrees, and she complained of fatigue. There was point tenderness over the bicipital groove of the right shoulder and tenderness of the skin lesions. The clinical impression was gonococcal bacteremia and she was treated with 10 million units of Aqueous Penicillin G intravenously per 24 hours. Overnight the lesions became less tender and less erythematous. Over the next four days the lesions resolved completely.

The first positive culture for gonorrhea was that taken from a 4 mm skin biopsy of a hemorrhagic pustule. This culture grew Neisseria gonococcus within two days. One week later only one of six blood cultures was positive for the organism. A cervical culture also became positive after one week. CTA sugars confirmed the specificity of the infections as Neisseria gonorrhea.

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*The Duluth Clinic, LTD, Duluth, Minnesota.

While in the hospital the patient was also started on Alkeran 4 mg. a day. Because she was in the hospital for further myeloma testing, and because of the wide dissemination of lesions, daily treatment, with 10 million units of Aqueous Penicillin IV was continued for 12 days.

Cultures from the cervix and rectum were negative during and two weeks following therapy. Her husband was treated, as a contact, with 4.8 million units of Procaine Penicillin and 1 gram of Probenecid. Pre-treatment pharyngeal, urethral and rectal cultures were negative.

No further contacts could be elicited.

Discussion

Patients with multiple myeloma, though not more susceptible to fungal infections, have an increased susceptibility to bacterial infections. The frequency of serious infections in previous studies has not correlated with neutropenia. Increased infections are thought to be due partially to decreased concentration of normal immunoglobulins. An increased breakdown of normal immunoglobulins has been demonstrated. A decreased serum antibody response is shown by the lower levels of antistreptolysin-O titer in plasma cell myeloma patients.[6] Cellular (Type 4, Gell-Coombs) hypersensitivity appears to be intact in plasma cell myeloma patients.[2]

Plasma cell myeloma patients have a markedly increased risk of serious bacterial infections of which pneumonia and pyelonephritis are the most common. In one recent study of hospitalized myeloma patients, gram negative bacteria predominated in the lung as well as urinary tract infections.[7] Earlier studies have indicated the diplococcus pneumoniae organisms were formerly most frequent in the lung. Previous comprehensive reviews of bacterial infections and multiple myeloma have not commented on the Neisseria infections,[2,7] except for one case report of Neisseria meningococcal septicemia.[4]

Patients with a typical gonococcal dermoarthritis syndrome usually present with a scant number of tender hemorrhagic pustules located on the distal parts of the extremities and are often associated with tenosynovitis. Because routine cultures done for organism confirmation are often negative, these patients are treated on the basis of a clinical diagnosis.

If available, direct immunofluorescence stains for Neisseria gonorrhea from a typical skin lesion biopsy provide a test for sensitive and rapid confirmation, but fluorescent antibody techniques are more cumbersome and not as reliable as appropriately performed cultures.[10]

About 50% of Gonococcal Bacteremias, which have negative blood, urethral and cervical cultures, may be confirmed by the addition of pharyngeal and rectal cultures.[5] A bacterial culture from a biopsied skin lesion provides a high yield of positive results, while a gram stain of the superficial pustule gives a low yield (10%).

Conclusion

A patient with previous undiagnosed plasma cell myeloma was admitted to the hospital for treatment of menorrhagia. While undergoing dilatation and curettage of the uterus, she developed generalized distribution of a large number (over 200) of tender pink lesions, which rapidly became hemorrhagic pustules. A clinical diagnosis of Gonococcal bacteremia was made. She had a rapid response to intravenous penicillin therapy.

The clinical impression was confirmed most rapidly by bacterial growth from the culture of a skin biopsy.

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Salt Load as a Trigger for Migraine

JOHN B. BRAINARD, M.D.*

Restriction of salt ingestion from snack foods on an empty stomach lowered the incidence of recurrent headaches in 10 out of 12 patients with proven migraine.

MIGRAINE IS A DEVASTATING affliction for millions of Americans. The discovery of a simple, easily controlled factor causing migraine attacks was deemed worthy of reporting.

The mechanism causing the pain of migraine has been shown[1] to be vasodilatation of cerebral blood vessels with an accompanying accumulation of a polypeptide in blood vessel walls and perivascular tissues. Dilated vessels cause pain, but the polypeptide is irritating to the surrounding tissues and causes extreme discomfort until it is either metabolized or neutralized by endogenous cortisone. The typical attack may last from a few hours to several days, depending on the severity of the vasodilatation and the amount of polypeptide accumulated.

In individuals susceptible to migraine, many factors are known to precipitate attacks. These factors include vasodilating chemicals like sodium nitrite, a food preservative which is the cause of "hot dog headache";[2] tyramine, which is the troublemaker in cheese and some wines;[4] and phenylethylamine, the probable offender in chocolate.[3]

Monosodium glutamate has been identified[5,6] as the cause of "Chinese restaurant syndrome" headache. Foods which commonly cause headaches are milk products, nuts (including coconut oil), pork and wheat. Specific offending chemicals have not been isolated in each food.

Other factors known to precipitate migraine are visual stimuli, viral or bacterial infections, surgical operations, high altitude, seasonal allergies and hypoglycemia.

A potent but previously undescribed trigger mechanism—a sudden sodium chloride load—was noted in several patients. In these patients, symptoms could be reproduced by oral administration of sodium chloride.

Material and Method

All patients were known to have had migraine headaches for many years and had been treated with and responded to ergotamine therapy. They were advised to avoid all the previously listed precipitating factors and to record their incidence of migraine headaches over a six month period before and after salt restriction. The salt restriction consisted of avoiding all salted snack foods, such as pretzels, nuts and potato chips before meals. Results were considered excellent if the patient was free of migraine, good if the incidence of headaches was reduced, and poor if no change was noted.

RESULTS
Response to Salt Restriction by Migraine Patients

Case	Response
1	Good
2	Excellent
3	Good
4	Poor
5	Excellent
6	Good
7	Good
8	Poor
9	Good
10	Good
11	Excellent
12	Good

Discussion

Most of the patients (10 out of 12) responded favorably. In a few, the results were quite dramatic with the patients stating that migraine was no longer a problem for them. It was not determined if the poor responders were impervious to sudden salt load or simply unable to avoid other known or unknown trigger factors.

The ubiquity of highly salted snack foods in our society may contribute to the presence of migraine. The individual who has found that chocolate causes headaches turns to snacking on potato

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St. Paul, Minnesota.

chips or crackers. The patients in this study had typical migraine, often being awakened by headaches in the night. The relief obtained suggests that sodium load requires several hours to precipitate a migraine. It has not been appreciated that the sudden salt load of a handful of salted nuts or potato chips, particularly if taken on an empty stomach, can cause a severe migraine six to twelve hours later. The reason for the lag period is unknown.

Summary

Migraine patients who stopped ingesting highly salted snack foods, while avoiding other previously described migraine triggers, were symptomatically improved in most cases.

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Request for Physician's Art Work

For many years the Board of Editors of MINNESOTA MEDICINE has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers have received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Pictures will be returned if identified with the name and address of the physician. Please submit your picture as prospective cover subjects to the Editor of MINNESOTA MEDICINE, 101 East 5th St., Suite 900, St. Paul, Minnesota 55101.

During 1976 the Editors would like to pay homage to the Bicentennial by having our covers depict places, events, objects, scenes, etc., that have historical or patriotic significance for the State of Minnesota. Please keep the Bicentennial theme in mind when submitting prospective covers for 1976.

Farrell Stiegler, M.D.
Cover Editor

Annual Meeting

6 + 6 + 1 = 13 . . . And if you take full advantage of the scientific program offerings at CME '76, 13 hours of continuing education will be yours for only $10 (nonmembers $25). It all adds up to Rochester, May 20-21.

Minnesota State Medical Association

Annual Meeting

Rochester—A Celebrated City

Attendees at this year's Annual Meeting have something in common with the Empress of Iran, European royalty, scores of political figures including several United States presidents, and more movie, television and Broadway stars than appeared in Ben Hur and Cleopatra combined. CME '76 in Rochester, Minnesota, brings you to the community which has welcomed thousands of V.I.P.'s. But Rochester offers much more than sharing her acquaintances with celebrities.

Rochester's charm begins with its scenic location amidst the beauty of the Zumbro River Valley. Rolling hills and a quiet countryside make one wish he were a Monet, capable of capturing such splendor on canvas. Midwestern friendliness and cosmopolitan amenities are combined with ingenuity. Apache Mall Shopping Center, a complex featuring three nationally-known department stores and dozens of specialty shops, is just a short hop by bus or cab. If you would rather fill your free hours with history, culture, and art, the Olmsted County Historical Society, Mayo Medical Museum, Rochester Art Center, the city's Civic Theater, and other landmarks beckon you to enjoy cultural samplings not unlike those found in much larger metropolitan areas.

If you get a chance, make your way to Silver Lake Park, haven for thousands of wild Canadian Geese. To make a hit with these Canadians pick up a bag of dried corn at the supermarket next to the lake.

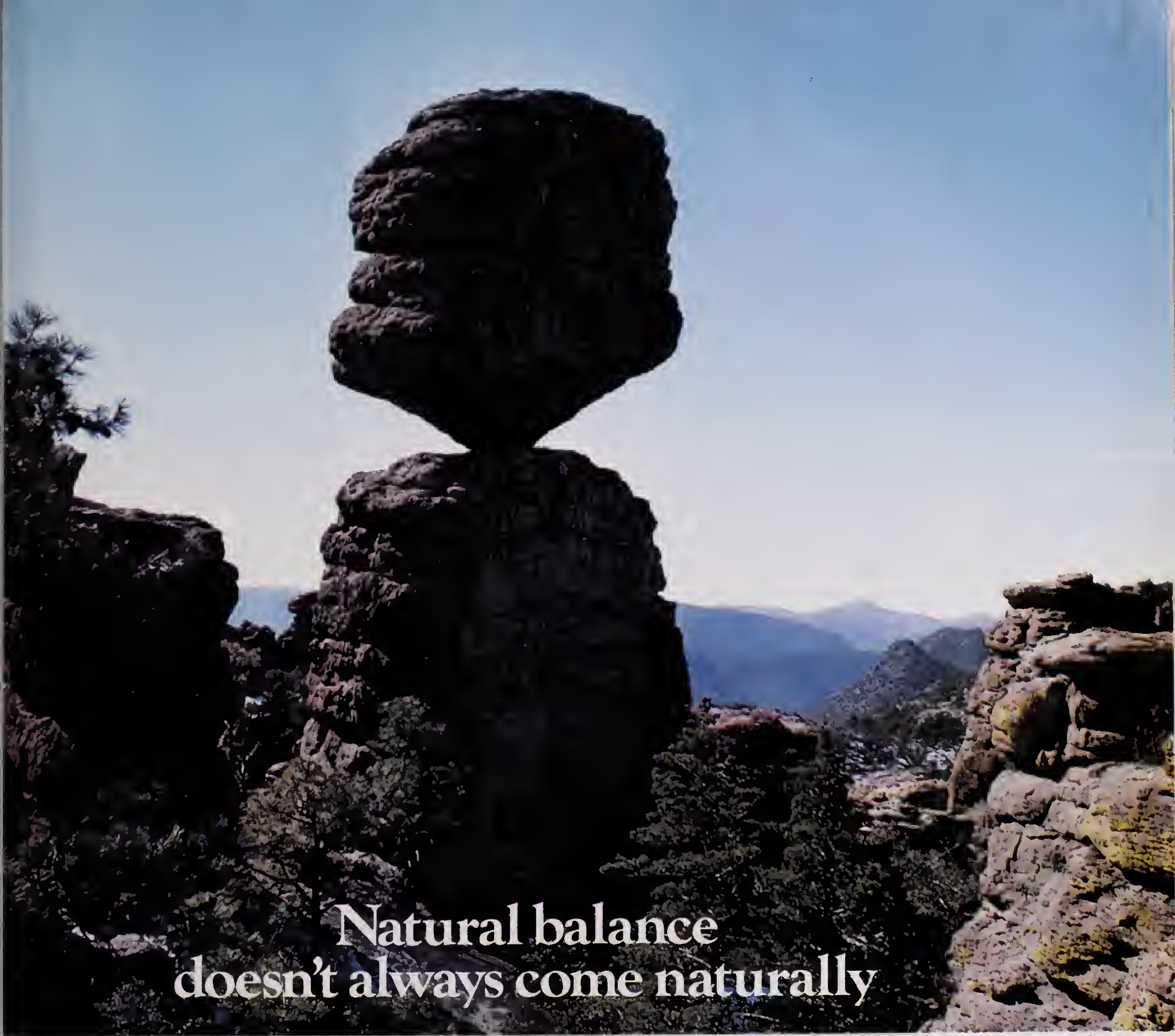
The many specialty shops, located on the subway level between the Kahler and the Clinic, tempt you with selections of imported and domestic clothing and gifts. And while you're in Rochester, why not "go through" the clinic? On a tour, that is. Informational tours of the Mayo complex are available twice daily. And Mayowood, formerly the family estate of Drs. Charles H. and Charles W. Mayo, is now a state historical site—its Victorian elegance should be appreciated by every visitor.

Dining in Rochester can be a unique experience. At last count, more than eighty restaurants offering as many different bills of fare invite you to enjoy their hospitality . . . Aptly christened, The Depot House lets you relive the glorious days when railroads were king and travel luxurious. Early reservations will assure you gourmet dining in a private railway coach . . . Michael's restaurant, located in the heart of the city on Broadway, serves the finest prime steaks . . . Bridget's, with the flair of an old English inn, is part of the Holiday Inn Downtown . . . In the Kahler Hotel, the Elizabethan Room with grace and elegance befitting its namesake era, and the Pinnacle Restaurant on the Roof with a panoramic view and exotic menu of open hearth cooking will make your dining choice a difficult one.

Just beyond the city limits The Fish House with a coastal atmosphere and seafood menu rivaling Cape Cod's finest is only ten miles south in Stuartville. Or, explore Mantorville, home of the famous Hubbell House, where great food and historical memorabilia abound. Mantorville is just fifteen miles west of CME '76 headquarters. For complete information on area happenings, consult the recreation specialist stationed on the mezzanine level of the Kahler Hotel.

Accept Rochester's invitation—and ours—to be a part of "Chirurgical and Medical Emergencies '76," the 123rd MSMA Annual Meeting. You may not be a celebrity, but we think the special way Rochester treats its visitors will make you feel like one.

R. D. Semsch, M.D. **Chairman** **Scientific Assembly**	**John G. Mayne, M.D.** **Chairman** **Local Arrangements**



Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

ound useful in the management of vertigo* associated with ases affecting the vestibular system.

an relieve nausea and vomiting often associated with vertigo.*

sual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.

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ntivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for sea, vomiting and dizziness associated with motion sickness.

F SUMMARY OF PRESCRIBING INFORMATION

NDICATIONS. Based on a review of this drug by the National Academy of iences—National Research Council and/or other information, FDA has classified e indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with otion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the stibular system.

Final classification of the less than effective indications requires further vestigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

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Effectiveness across the spectrum of most common forms of insomnia

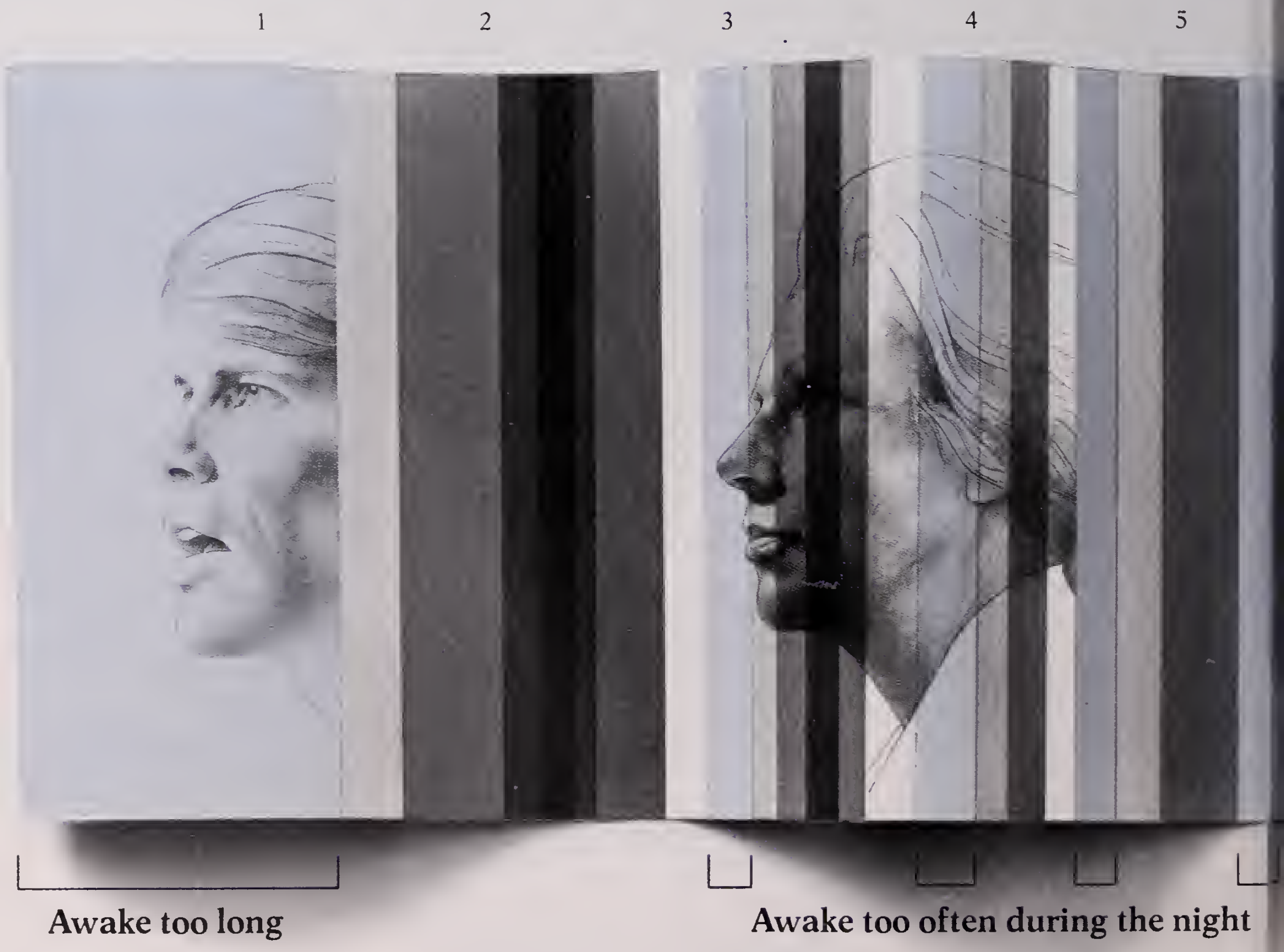
Awake too long, awake too often, awake too early...

These are the most common forms of insomnia, and may occur singly or in any combination. The night of troubled sleep depicted here comprises all three types. As the night progresses from left to right, each sleep stage is identifiable by its own shade of gray. Blue represents "Awake."

As you can see, this hypothetical "patient" takes well over an hour to fall asleep, awakens several times during the middle of the night and awakens too early in the morning.

Sleep Stages

▢ Awake
□ REM
░ Stage 1
▒ Stage 2
▓ Stage 3
█ Stage 4

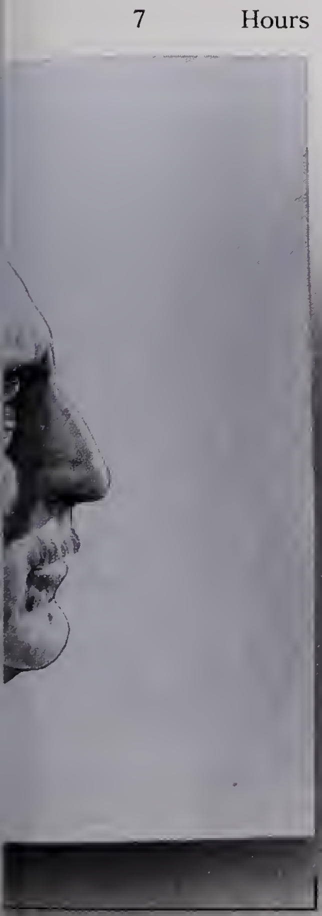


The insomnias most often occurring in young and older adults

For patients with trouble falling asleep (common in young adult insomnia patients), Dalmane (flurazepam HCl) 30 mg provides sleep within 17 minutes, on average. For those with trouble staying asleep or sleeping long enough (common in those over 50), Dalmane offers increased total sleep time with fewer nocturnal awakenings. These clinical results were demonstrated in studies conducted in four geographically separated sleep research laboratories.[1-4]

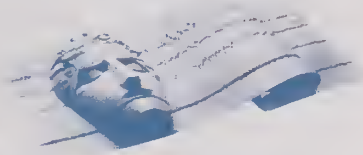
The relative safety of Dalmane (flurazepam HCl) is well documented

Dalmane (flurazepam HCl) is relatively safe and well tolerated; morning "hang-over" has been infrequent. The usual adult dosage is 30 mg; in elderly or debilitated patients, limit initial dosage to 15 mg to preclude over-sedation, dizziness or ataxia. Caution patients about possible combined effects with alcohol and other CNS depressants.



Awake too early

Broad-spectrum medication for the most common forms of insomnia



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One 30-mg capsule *h.s.*— usual adult dosage (15 mg may suffice in some patients).
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☐ induces sleep rapidly
☐ reduces nighttime awakenings
☐ lengthens total sleep time

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Please see following page for a summary of complete product information.

Broad-spectrum medication for the most common forms of insomnia

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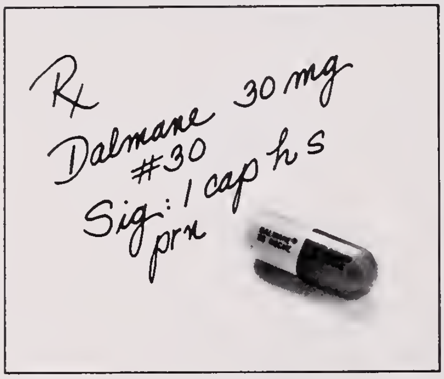

Objectively proved in the sleep research laboratory, Dalmane

☐ induces sleep within 17 minutes, on average
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Before prescribing Dalmane (flurazepam HCl), please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum benef effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

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Editorials

"Stroke: What's New? Cerebral Revascularization"

Dr. Ausman and his colleagues* are to be complimented for their concise report regarding their experience with cerebral revascularization. They indicate that this is a new procedure, and much like coronary revascularization, must withstand the test of time. It is apparent that it is technically feasible to anastomose a superficial temporal artery to a branch of the middle cerebral artery and obtain a patent anastomosis in the vast majority of cases. One of the major problems related to this operation is the varying indications given for the procedure and the marked differences in the criteria employed to evaluate these patients pre- and postoperatively.

A review of our 41 bypass procedures of this nature performed to date reveals major common grounds but also some differences in opinion regarding the indications for the procedure. In our judgment this operation has been indicated primarily for relatively uncommon manifestations of cerebral vascular disease. The surgery has been performed for the "slow stroke," progressing strokes, transient ischemic attacks persisting after carotid occlusion or related to a middle cerebral artery stenosis, generalized cerebral ischemia, and for the purpose of bypassing the internal carotid artery for giant aneurysms arising from that vessel which are not considered operable by other techniques. Early in our experience we did indeed perform this surgery for patients who had sustained a recent completed infarction, but we found no improvement from the operation in such people and have abandoned it for the type of individual described in their Case 2. We do not feel that a bypass procedure is required for an occluded carotid artery that is asymptomatic prior to endarterectomy on the contralateral vessel. Appropriate monitoring techniques and shunting as required have markedly reduced the risks of surgery in these patients. The risks of additional surgery in these patients is not frequently justified in our judgment.

The indications for this operation for people with dementia is certainly subject to controversy. Dementia or difficulty with cerebration has formed a portion of the syndrome we have described as generalized cerebral ischemia, but it is only one component of a syndrome that is restricted to patients with bilateral internal carotid artery occlusions, markedly reduced retinal artery pressures, lethargy, and frequent episodes of syncope related to upright position. The authors point out that progressive dementia in adults may occasionally be due to occlusive vascular disease, we would support this statement, but caution that, in our judgment, occlusive vascular disease in vessels that can be bypassed is an uncommon cause for dementia.

I was particularly impressed by the authors' case relating to the anastomosis of the occipital artery to the posterior inferior cerebellar artery. To my knowledge, this is the first reported case of this nature and certainly offers some possibilities for helping patients with vertebral artery disease.

It now appears that the major challenge referable to this operation will be related to the identification of the indications for the surgery. Its technical feasibility has been proven; its role has not. Articles of the type reported by Dr. Ausman and his associates should make this determination possible.

Thoralf M. Sundt, Jr., M.D.†
Rochester, Minnesota

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*See page 223.

†Department of Neurologic Surgery, Mayo Clinic.

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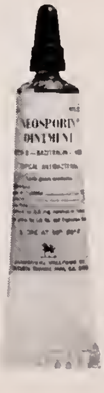
Complete literature available on request from Professional Services Dept. PML.



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Hennepin County Doctor's Directory

In 1975 the Hennepin County Medical Society Health Coalition worked together to develop and publish a *Directory of Primary Care Physicians*. Directories have been published before, in other areas of the country, but their value was lessened by militant consumer groups fighting with conservative medical societies. Our Hennepin County effort was the first time in the nation that a medical society and consumer groups cooperated to publish a directory of value for patients seeking a doctor.

Medical response to the Directory was excellent. Four hundred ninety-five out of 596 primary care physicians responded to the survey and were listed in the Directory. The Directory was limited to Hennepin County Primary Care Physicians, so not all doctors who wanted to be were listed. There was confusion as to what is a "Primary Care Physician"? Excerpts from the American Academy of Family Physician's definition may help: "Primary physicians give first contact medical care *and* assume continuing responsibility for the patient. The care which they give is both personnal and comprehensive." Pediatricians, General Practitioners, Internists and Gynecologists are all primary physicians.

Family Physicians are also primary care physicians. "Their unique attitudes, training and experience qualify them to practice in the several fields of medicine and surgery and enable them to provide care to the entire family regardless of age, sex or type of problem. A family physician also serves as the patient's advocate in all health related matters."

Patient response to the Directory has also been excellent. Nineteen thousand copies were printed for $8,000. Except for reference copies they are all gone from the Minneapolis Libraries. The county libraries still have copies, as does the County Medical Society and the Community Health and Welfare Council.

Both organizations use their supply to send to people who call each day looking for a doctor; particularly people new to the community who have not yet found a primary care physician.

Nationally the Directory has also been a success. Our state, the Coalition for Health Care and the Hennepin County Medical Society have all received favorable publicity; nationally in the medical press and locally in the area newspapers. Requests for the Directory and for the Physician Questionnaire have been received from California, Texas, Florida, Pennsylvania and from many other states.

Medicine in Minnesota has again been a leader in patient care. The physicians of this state are to be congratulated for their flexibility and their willing cooperation in testing innovations such as this which may improve health care . . . health care, not only for their own patients which is already outstanding but care also for patients in general, which includes a small minority who do not yet have a primary care physician.

John E. Smith, M.D.
Minneapolis, Minnesota

Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

1. Preferably an alumnus of the University of Minnesota Medical School.
2. Not engaged in an academic capacity.
3. Has made outstanding contributions to the Medical School, the University, the Alumni Association or the community at large.
4. Have a relatively long experience in the field of medical science or a related field.

Nominations for the 1976 awards should be sent immediately to:

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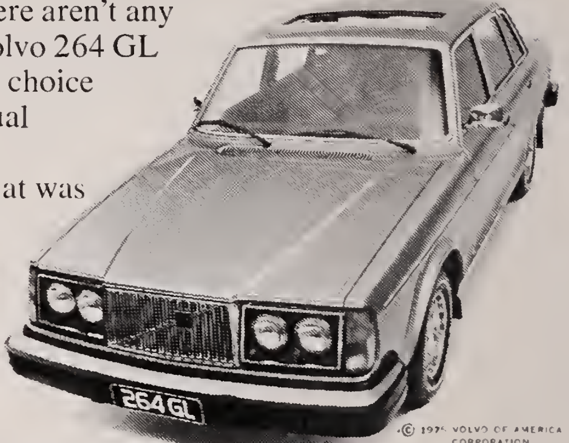

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Urethritis Associated with Chlamydia

Clinicians have speculated as to the causative nature of so-called non-specific urethritis when tests for specific micro-organisms, such as gonococcus, have been negative.

Various causes have been implicated—bacteria, viruses, yeasts and protozoans. Cultures and stains have been variable and inconsistent.

Weed et al.* have found a rather high incidence of Chlamydia (23%) in non-specific urethritis when special culture techniques are employed. They also observed excellent clinical response when treated with tetracycline.

A clinician's first concern in urethritis is to rule out gonorrhea, then trichomonas, yeast infection and then non-specific organisms. At the present time, most laboratories are not equipped to culture viruses and Chlamydia. In any case, it is reassuring to know from the studies at the Mayo Clinic that Chlamydia responds to tetracycline therapy. That has been the drug generally employed successfully in non-specific urethritis when the cause was not known.

The authors are to be commended for their investigation of this common but sometimes perplexing problem.

Gordon W. Strom, M.D.
Minneapolis, Minnesota

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*See page 228.

Letters to the Editor

To the Editor:

Soviet Jewish Physicians

Over the past several months, there has been increasing world concern over the fate of Soviet Jewish physicians, scientists, and intellectuals who have sought to emigrate to Israel and elsewhere. Often dismissed from their jobs, barred from their laboratories, or demoted to menial tasks, they live with the fear that they will be arrested or imprisoned, perhaps in a mental hospital,[1] or that permission to emigrate will never be granted to them. Some case histories will illustrate:

—Dr. Mikhail Shtern, former Chief of Endocrinology at Vinnitsa Hospital in the Ukraine, was recently sentenced to eight years imprisonment for accepting "bribes" from his patients. Leading Western jurists have stated that the fact that Shtern's two sons had applied to go to Israel had much more to do with his conviction than any violation of Soviet law.[2]

—Dr. Ilya Glezer, noted neuroanatomist, is now serving the last three years of a six-year prison term for alleged "anti-Soviet propaganda". His crime consisted of writing a letter concerning Soviet anti-semitism.[3]

There are other physicians imprisoned, and still more denied the right to practice since requesting exit visas. The Western medical community must now demand the rights of free emigration and freedom to practice without harassment because of one's personal beliefs for their colleagues in the Soviet Union. Western physicians planning to travel to Russia can be particularly effective by raising these issues with their Russian hosts, and by pointing out that if scientific and technical interchange is to continue with the West, it must be based on the principle of respect for human rights, not on intimidation. Further information concerning these and other violations of the rights of Soviet Jews, as well as suggestions for action, may be obtained from the Medical Mobilization for Soviet Jewry, 233 Bay State Road, Boston, Mass. 02215.

Lauro F. Cavazos, Ph.D.*
Paul Reich, M.D.†
Boston, Mass.

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*Tufts University School of Medicine.
†Department of Medicine, Harvard Medical School.

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Letters to the Editor

Dear Editor:

Asbestos in Duluth Water—
A Rebuttal of a Revision

James R. Coleman is logical in much of his criticism (Duluth Water Revised)[1] of the mechanical aspects of the presentation, "Asbestos in Duluth Water."[2] As stated in this article, I had no first hand knowledge of these matters and sought out the most dependable source of the information at the National Water Quality Laboratory in Duluth. No one or group of scientists has anywhere near the daily full time experience of studying the nature, source, concentration and treatment of it after they discovered the asbestos in Lake Superior water.[3]

According to Coleman, there are three principle mistakes in the mechanical and mathematical aspects of my presentation. For the sake of brevity and in the interest of the readers, I will discuss these three points separately and collectively, using today's rapidly growing knowledge in this field.

Coleman's first criticism concerned the use of the figures 20 to 70 million asbestos fibers per liter in Duluth's tap water. He cited other experts who found 1 to 10 million and another 1.1 to 4.8 million. During the last year the groups at NWQL and Mt. Siani School of Medicine published their determination of an average amphibole fiber concentration of 40 to 100 million with a range of 10 to 1000 million fibers per liter.[4] It's obvious that a universally agreed to procedure both accurate and easily duplicated for counting and identifying asbestos fibers remains an enigma.

Coleman's second criticism concerned the exact nature of the asbestos fibers in the tap water implying that there are sources other than the 67,000 tons of waste dumped daily into Lake Superior by the Reserve Mining Company at Silver Bay. The scientists of the NWQL have made extensive studies of the lake and its tributaries and find no other significant source of its amphibole fibers. These are frequently identified as to their exact nature by x-ray diffraction and electron beam analysis before they are counted. A discussion of the complicated chemistry of the amphiboles and the interrelated terms used in manufacturing plants is not essential to identifying the source of these fibers in the lake. As to the pathogenicity of the amphiboles there is in addition to the original references a new study "Morbidity and Mortality Among Hard Rock Miners Exposed to Asbestiform Mineral" by Gillam et al.[5] They reveal a significant carcinogenic action of inhaled amphiboles from cummingtonite-grunerite minerals similar to those dumped into Lake Superior. This carcinogenic effect is in spite of a very low concentration of only two fibers of more than 5 μm in length per cubic centimeter of air inhaled by these deep mine workers in South Dakota.

Lastly, in reference to the "mathematics of the potential hazard" Coleman states, "It must be pointed out that this standard is related to the number of fibers greater than 5 μm in length only and it appears that Dr. Wells has overlooked the fact." Now either Coleman read my calculations and references only superficially or he had other reasons for making this misstatement of fact. I did use a conversion factor of three recommended in PLO Publications, 27 pp 37 Geneva 1972 to convert the number of fibers from 450x to 7000x for amosite. I am now told at NWQL that this was an error, that the conversion factor is more like 20 times.

What are we arguing about? The big question is: "can ingested asbestos fibers be injurious to health and if so, what is the maximum concentration which is safe?" There is no known answer to the last question. To the first, one must consider the five large group studies of workers exposed to inhaled asbestos dust—originally referred to in last June's issue of our Journal.[1] These men developed, besides mesotheliomas and cancer of the lungs, three times more cancer of the gastrointestinal tract than others in the same age bracket. To my knowledge no one has yet proved that ingested asbestos fibers in drinking water will kill. In spite of almost universal exposure of man to inhaled and ingested asbestos, the 120,000 people in the Duluth area are being unnecessarily exposed to a dangerous concentration of asbestos in their drinking water.

It must be pointed out that with almost every statement which occurs in the courts of law or in the news media contrary to the beliefs or benefits of the mining company, there follows a rebuttal, generally by someone in some way connected with the company. There is relatively little control of testimony in the courts or in the news media, but in the case of a scientific publication in a scientific medical journal, there is no excuse for a criticism being published without at least the courtesy to the reader and in fairness to the original author of a response in the same issue.*

I would be remiss in not briefly bringing the readers up to date on the recent developments in Duluth. The filter plant should be satisfactorily clearing our city water of most of the asbestos in about one year. This will cost roughly in excess of six million dollars. Practically every restaurant and large hotel here now serves controlled filtered water. Cartons of "free" well water are now available at numerous sites. This water is now delivered to shut-ins. Satisfactory water filters are available at a reasonable cost for private homes. All this does not mean that all business men and physicians agree as to the possible dangers. To date, one large hospital does not filter its drinking water, probably because of the number of physicians who feel that "too much has been made of the subject."

Practically all the expenses of creating the greatly improved conditions in this city were to be covered by you, the taxpayer. Since Reserve's officials originally agreed to be responsible for damage their tailings might do, Federal Judge Devitt ruled that the mining company must cover much of this expense. There remains a decision as to who will pay for the permanent filtering plants.

Arthur H. Wells, M.D.
4640 London Road
Duluth, Minnesota

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*Editors Note: We agree with Dr. Wells about this point. This was an oversite on our part.

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1. Coleman JR: Duluth water revised. Minnesota Med 59:95, 1976.
2. Wells AH: Asbestos in Duluth water. Minnesota Med 458:58, 1975.
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5. Gillam JD, Dement J, Lemen RA, Wagoner JK and Archer VE: Morbidity and mortality among hard rock miners exposed to an asbestiform mineral. Presented at New York Academy of Sciences, Conference on Occupational Carcinogenesis, Mar 24, 1975. To be published.

Continuing Medical Education
Minnesota Society of Anesthesiologists

1976 Spring Scientific and Business Meeting, April 10, Marriott Motor Inn, Bloomington. Subjects: Life Support Systems and History & Development of the Sanders Ventilator. Contact: Charles J. Restall, M.D., Mayo Clinic, Rochester.

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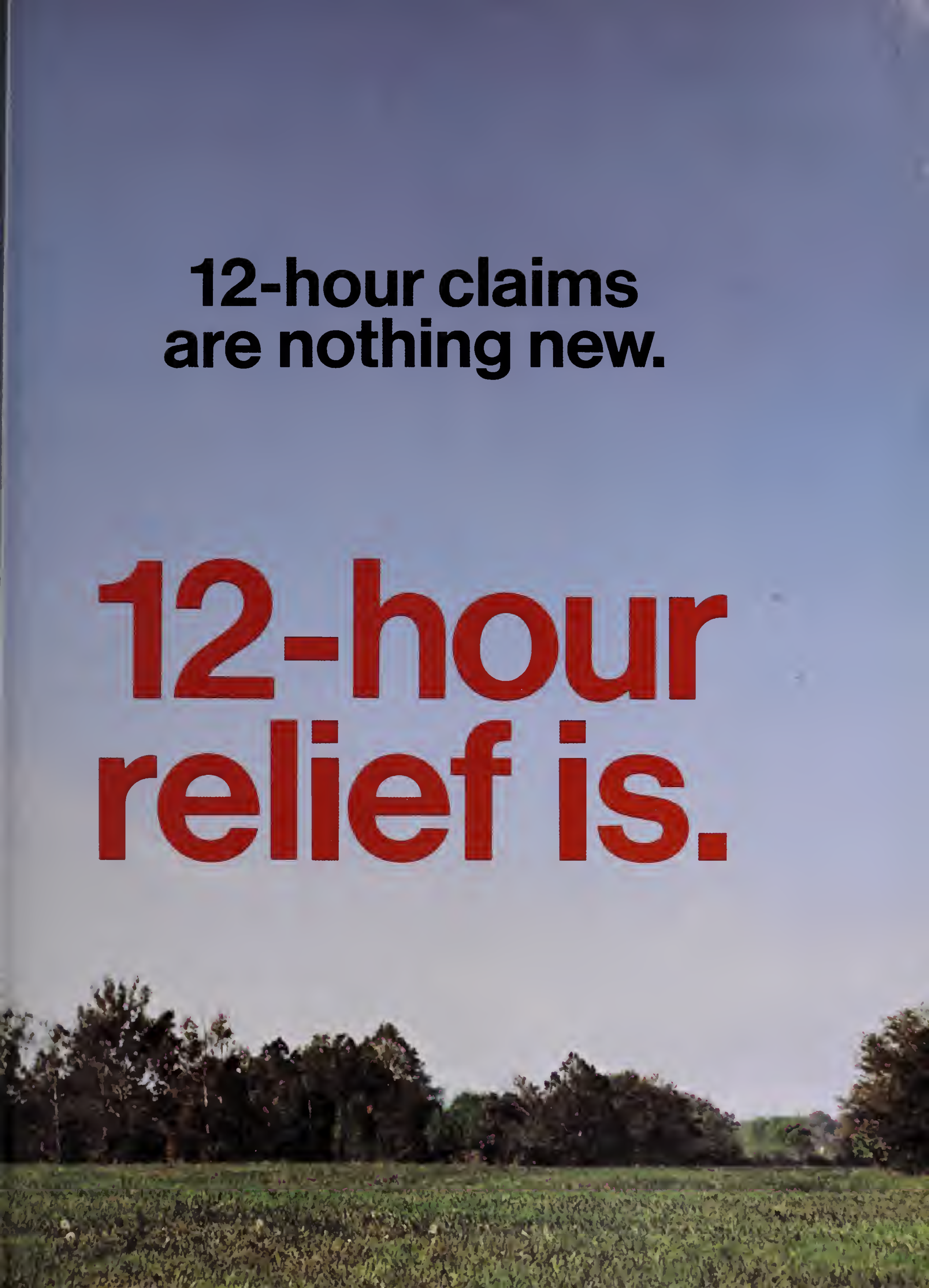
(Continued to page 276)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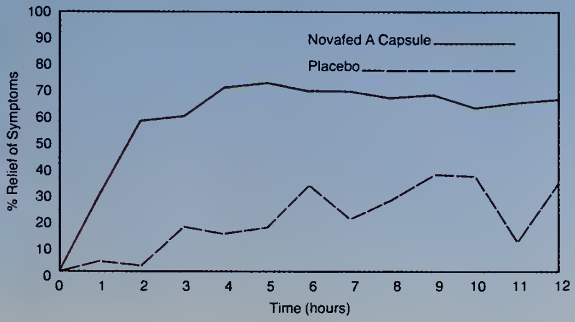

*Unpublished data, Medical Department Files, Dow Pharmaceuticals, The Dow Chemical Company, Indianapolis, Indiana.

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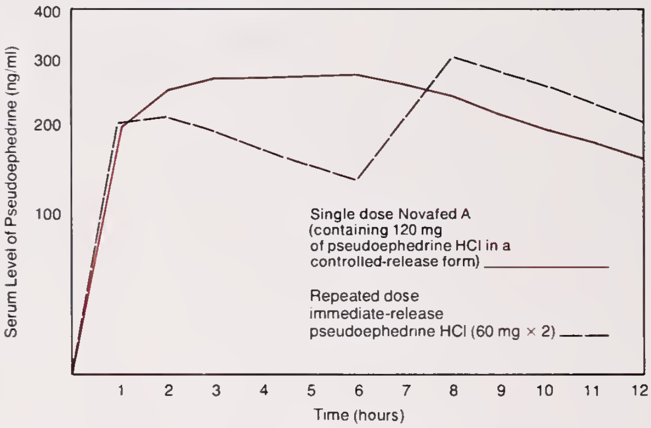
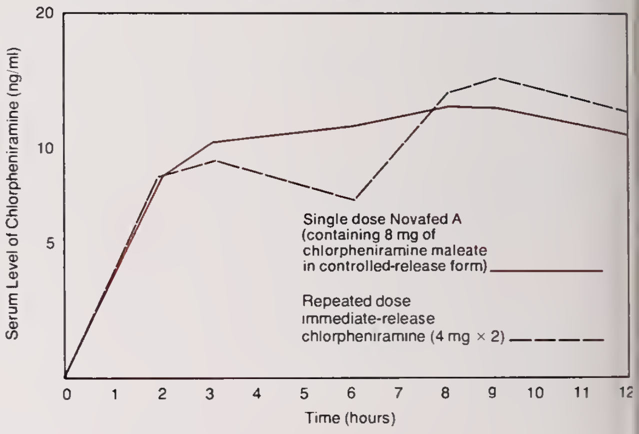


Comparison of Mean Serum Levels of Chlorpheniramine Following Novafed A and an Immediate-Release Reference Formulation*



*Unpublished data, Medical Department Files, Dow Pharmaceuticals, The Dow Chemical Company, Indianapolis, Indiana.

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ACTIONS: NOVAFED A combines the action of a nasal decongestant, pseudoephedrine hydrochloride, and an antihistamine, chlorpheniramine maleate. These ingredients are combined to provide prompt and sustained nasal and upper respiratory decongestant and antihistaminic action.

INDICATIONS: NOVAFED A is indicated for the relief of nasal congestion and eustachian tube congestion associated with the common cold, sinusitis and acute upper respiratory infections. It is also indicated for perennial and seasonal allergic rhinitis, vasomotor rhinitis, allergic conjunctivitis due to inhalant allergens and foods and for mild, uncomplicated allergic skin manifestations of urticaria and angioedema. Decongestants in combination with antihistamines have been used for many years to relieve eustachian tube congestion associated with acute eustachian salpingitis, aerotitis media, acute otitis media and serous otitis media. NOVAFED A may be given concurrently, when indicated, with analgesics and antibiotics.

CONTRAINDICATIONS: Symphathomimetic amines are contraindicated in patients with severe hypertension, severe coronary artery disease, and in patients on MAO inhibitor therapy. Antihistamines are contraindicated in patients with narrow-angle glaucoma, urinary retention, peptic ulcer, during an asthmatic attack, and in patients receiving MAO inhibitors.

Children under 12: NOVAFED A controlled-release capsules should not be used in children less than 12 years of age.

Nursing Mothers: Pseudoephedrine is contraindicated in nursing mothers because of the higher than usual risk for infants from sympathomimetic amines.

Hypersensitivity: This drug is contraindicated in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines or antihistamines. Patient idiosyncrasy to adrenergic agents may be manifested by insomnia, dizziness, weakness, tremor or arrhythmias.

WARNINGS: Sympathomimetic amines should be used judiciously and sparingly in patients with hypertension, diabetes mellitus, ischemic heart disease, increased intraocular pressure, hyperthyroidism, or prostatic hypertrophy. Sympathomimetics may produce central nervous system stimulation and convulsions or cardiovascular collapse with accompanying hypotension.

Antihistamines may impair mental and physical abilities required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery, and mental alertness in children. Chlorpheniramine maleate has an atropine-like action and should be used with caution in patients with increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension or in patients with a history of bronchial asthma.

Do not exceed recommended dosage.

Use in Pregnancy: The safety of pseudoephedrine for use during pregnancy has not been established.

Use In Elderly: The elderly (60 years and older) are more likely to have adverse reaction to sympathomimetics. Overdosage of sympathomimetics in this age group may cause hallucinations, convulsions, CNS depression, and death. Therefore, safe use of a short-acting sympathomimetic should be demonstrated in the individual elderly patient before considering the use of a sustained-action formulation.

PRECAUTIONS: This drug should be used with caution in patients with diabetes, hypertension, cardiovascular disease and hyperreactivity to ephedrine. The antihistaminic may cause drowsiness and ambulatory patients who operate machinery or motor vehicles should be cautioned accordingly.

ADVERSE REACTIONS: Hyperreactive individuals may display ephedrine-like reactions such as tachycardia, palpitations, headache, dizziness, or nausea. Patients sensitive to antihistamines may experience mild sedation.

Sympathomimetic drugs have been associated with certain untoward reactions including fear, anxiety, tenseness, restlessness, tremor, weakness, pallor, respiratory difficulty, dysuria, insomnia, hallucinations, convulsions, CNS depression, arrhythmias, and cardiovascular collapse with hypotension.

Possible side effects of antihistamines are drowsiness, restlessness, dizziness, weakness, dry mouth, anorexia, nausea, headache and nervousness, blurring of vision, heartburn, dysuria and very rarely, dermatitis.

DRUG INTERACTIONS: MAO inhibitors and beta adrenergic blockers increase the effect of sympathomimetics. Sympathomimetics may reduce the antihypertensive effects of methyldopa, mecamylamine, reserpine and veratrum alkaloids. Concomitant use of antihistamines with alcohol tricyclic antidepressants, barbiturates and other central nervous system depressants may have an additive effect.

DOSAGE AND ADMINISTRATION: One capsule every 12 hours. Do not give to children under 12 years of age.

CAUTION: Federal law prohibits dispensing without prescription.

HOW SUPPLIED: NOVAFED A is supplied in red and orang colored hard gelatin capsules, monogrammed with the Dow diamond followed by the number 109, in bottles of 100.

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Minnesota State Medical Association Nominees for State Offices

In cooperation with the House of Delegates, we are publishing short biographies of the nominees for Minnesota State Medical Association offices. In addition, any delegate may make nominations from the House of Delegates floor after the report of the Nominating Committee.

Each elected official will assume his position at the conclusion of the 1976 Annual Meeting. The current president-elect, Dr. Richard Anonsen, was elected in 1975 and will become president after the 1976 Annual Meeting concludes.

President-Elect

Chester A. Anderson, M.D.

Since 1972, Doctor Chester A. Anderson has chaired the Association's Public Policy Committee. He has been a member of the Family Practice Committee and the Committee on Medical School Relations. He serves as a delegate to the House from the Mid-Minnesota Medical Society.

Doctor Anderson has been a family physician in Hector for 27 years. He is active in the Minnesota Academy of Family Physicians and has held most offices of the organization. He was president in 1970, and in 1974 received its Merit Award.

Doctor Anderson is a Diplomate, American Board of Family Physicians, and a Charter Fellow, American Academy of Family Physicians.

First Vice-President

Malcolm M. Fifield, M.D.

Doctor Malcolm M. Fifield is board certified in urology and practices in Duluth with two associates. He is on the staffs of St. Luke's Hospital where he was chief of staff in 1973, St. Mary's Hospital, and Miller-Dwan Hospital. With the opening of the medical school in Duluth, Doctor Fifield became clinical associate professor of urology.

He was president of the St. Louis County Medical Society in 1970 and has been a delegate to the Minnesota State Medical Association for the past six years. Currently he is chairman of the Association's Judicial Committee.

Doctor Fifield lists membership in the Minnesota Surgical Society, and the American Urological Association. He is also a member of the Interurban Academy of Medicine and the Duluth Surgical Society which he served as president in 1968. He serves on the executive council of the Minnesota Chapter, American College of Surgeons, and for three years he was on the executive committee of the North Central Section of the American Urological Association.

Thomas M. Recht, M.D.

Doctor Thomas M. Recht, Minneapolis, often serves as a delegate to the House of Delegates from the Hennepin County Medical Society and is a board member of his society.

With the Association, he has served on the Subcommittee on Standards of Medical Care and is currently on the Permanent Evaluation Committee.

Board certified in internal medicine, Doctor Recht is a member of the Minneapolis Society of Internal Medicine and the Minneapolis Academy of Medicine. He is a clinical assistant professor of internal medicine at the University of Minnesota Medical School.

Doctor Recht served as treasurer and board member of the Foundation for Health Care Evaluation from its founding until October, 1975.

Leslie A. Syverson, M.D.

Doctor Leslie A. Syverson has been a family physician with the Fergus Falls Medical Group for about 18 years. During this time, he has maintained a special interest in physical medicine and has actively assisted students interested in family medicine. He is assistant clinical professor in the Department of Family Practice University of Minnesota, and has served as a preceptor for students in the Rural Physician Associate Program and for other students on a short term basis.

Doctor Syverson has served the Park Region District and County Medical Society as delegate to the House of Delegates for the past five years. In 1970-72, he was also secretary of the Park Region District and County Medical Society.

Second Vice-President

John G. Mayne, M.D.

For Doctor John G. Mayne, board certified in internal medicine, rheumatology is a special interest. Currently, he is a consultant in the Division of Rheumatology and Internal Medicine at the Mayo Clinic. He is a member of the Association Committee on Rheumatic Diseases which he chaired for four years and a member of the American Rheumatism Association and the Minnesota and National Arthritis Foundations. He is an organizing member and medical advisor of the Arthritis Volunteer Action Committee of Olmsted County.

With the Association, Doctor Mayne has also been a member of the Scientific Assembly Committee and often serves as a delegate or alternate delegate to the House from the Zumbro Valley Medical Society.

He is a fellow, American College of Physicians, and an associate professor of medicine at the Mayo Graduate School of Medicine.

Secretary

David W. Anderson, M.D.

Doctor David W. Anderson, dermatologist, has practiced in St. Paul for the past 10 years. He was board certified in 1967 and has been very active in local and national dermatological organizations. He is a member of the American Academy of Dermatology, North American Clinical Dermatological Society, and the Masters Dermatological Society. Currently, he serves as president of the Minnesota State Dermatological Society.

In addition, Doctor Anderson is a member of the Medical Assembly of St. Paul and current president of the Clinical Club of St. Paul. As a member of the Ramsey County Medical Society, he has served on its Grievance Committee and Executive Board. He is a MINNPAC member.

Doctor Anderson is an associate clinical instructor in dermatology at the University of Minnesota and an instructor in the family practice program at Bethesda Hospital, St. Paul.

Vincent E. Eilers, M.D.

For the past four years, Doctor Vincent E. Eilers has been a Ramsey County Medical Society delegate to the Association House.

An orthopaedic surgeon, Doctor Eilers was board certified in 1968. He is a member of the American Academy of Orthopaedic Surgeons, American College of Surgeons, St. Paul Surgical Society, Pan American Medical Association, and the Twin City Orthopaedic Society which he served as secretary for a year. He is an assistant clinical professor in orthopaedic surgery at the University of Minnesota Medical School and in 1975 served as chief of staff at Samaritan Hospital, St. Paul.

Treasurer

Joseph A. Cella, M.D.

Doctor Joseph A. Cella, Minneapolis, has combined a special interest in cancer and breast cancer screening with his specialty, obstetrics and gynecology.

In 1956-57, he served a year's clinical fellowship with the American Cancer Society at Mercy Hospital, Minneapolis. Since that time, he has been active in the work of the Society, currently serving as president of the Hennepin County Unit. As part of his society activities, he lectures under its public health program.

Doctor Cella is board certified by the American Board of Obstetrics and Gynecology and is a member of the American College of Obstetricians and Gynecologists. He is also associate clinical instructor of obstetrics and gynecology at the University of Minnesota.

James C. Mankey, M.D.

Current Treasurer of the Association, Doctor James C. Mankey has served the Association as first vice president in 1974. A long active member, Doctor Mankey has served on the Committees on Interprofessional Relations; Medical School Relations; Residents, Interns and Medical Students; Scholarship and Loans and Laboratory Practice and Blood Banks.

A Minneapolis native, Doctor Mankey now serves the Mill City as internist.

He is a past secretary and past president of the Hennepin County Medical Society and a member of the American Medical Association, Minnesota Society of Internal Medicine, and Minneapolis Society of Internal Medicine.

He is board certified in internal medicine and is a fellow in the American College of Physicians. He is a clinical assistant professor at the University of Minnesota Medical School.

Speaker of the House

James W. Halvorson, M.D.

Current Speaker of the House of Delegates, Doctor James W. Halvorson, Zumbrota, was Association vice president, 1971-72, and vice speaker, 1974-75.

He is a member of the Committees on Automotive Injuries; Interns, Residents and Medical Students and Mental Health and its Subcommittee on Alcoholism and Other Chemical Dependencies. He is chairman of the Association sponsored Discussion Group Concerned with the Alcohol-Impaired Driver and Highway Safety and on the Board of Editors of MINNESOTA MEDICINE.

Known for his work combatting alcoholism and in programs relating to the drinking driver, Doctor Halvorson was given the AAA Service to Motoring Award in 1972. He is vice president of the Minnesota Council on Alcohol Problems and serves on the Advisory Committee to the Hennepin County Alcohol Safety Action Project.

Doctor Halvorson has been in family practice in Zumbrota for nearly 20 years and is a Diplomate, American Board of Family Practice, and a Charter Fellow, American Academy of Family Physicians. He is a member and past president of the Goodhue County Medical Society which he long has served as delegate to the House of Delegates.

Richard K. Simmons, M.D.

Minnesota born Doctor Richard K. Simmons is currently in family practice in Bloomington. He is a diplomate, American Board of Family Practice and has been very active in local and state chapters of the Academy of Family Physicians.

He served as treasurer, vice president and president of the Hennepin County Academy of Family Physicians. Currently, Doctor Simmons is speaker of the house of delegates and a member of the board of directors of the Minnesota Academy of Family Physicians. In addition, he has done some committee work with the Minnesota Academy and is currently a member of the Scientific Assembly Committee of the American Academy of Family Physicians.

Doctor Simmons is on the board of directors of the Hennepin County Medical Society and this past year served as a delegate to the MSMA House. He has served on the Association Child Health Committee and is currently on the Family Practice Committee.

Vice-Speaker of the House

Donald R. Jorgensen, M.D.

Doctor Donald Jorgensen, Willmar ophthalmologist, is the immediate past president of the Mid-Minnesota Medical Society and a fellow in the American College of Surgeons.

In addition, he holds memberships in 15 medical societies including the American Academy of Ophthalmology and Otolaryngology, Norsk Oftalmologist Forening (Norwegian Ophthalmological Society), American Board of Ophthalmology, and American Association for the Advancement of Science. In 1972 he was president of the St. Paul Ophthalmological Society, and in 1974 served as chief of staff, Rice Memorial Hospital, Willmar.

Doctor Jorgensen was in private practice in St. Paul for six years prior to moving to Willmar in 1972. In St. Paul, he served as chairman of the Clinical Department of Ophthalmology at the Charles T. Miller Hospital.

Severin H. Koop, Jr., M.D.

Doctor Severin H. Koop, Jr., St. Cloud, is the current vice-speaker of the House of Delegates. A board certified otolaryngologist, Doctor Koop is president of the Minnesota Academy of Ophthalmology and Otolaryngology. He is also clinical assistant professor at the University of Minnesota Department of Otolaryngology.

With the Association, Doctor Koop has been a member of the Committees on Conservation of Hearing and Medical School Relations and was first vice-president in 1973.

He lists membership in the Stearns-Benton County Medical Society, American Medical Association, and American Academy of Ophthalmology and Otolaryngology. In addition, he is on the Council of Otolaryngology of the American Academy of Ophthalmology and Otolaryngology.

Bruce E. Linderholm, M.D.

For two months during 1968, Doctor Bruce E. Linderholm served on the hospital ship, S.S. Hope, while it was stationed at Colombo, Ceylon. There, he and other ship staff taught American medical advancements.

A Minneapolis urologist, Doctor Linderholm is a member of the Minnesota Urological Association; the American Urological Association, North Central Section, and the American Urological Association. He is certified by the American Board of Urology and currently serves as co-chief of urology at Hennepin County General Hospital.

In 1974, Doctor Linderholm was president of the Hennepin County Medical Society and in 1975, was chairman of its board of directors.

Annual Meeting—Rochester—May 20 & 21

Remember the fun we had at last year's Bavarian Beer Fest? We're planning another great, relaxing event for the finishing touch to CME '76. On Friday, May 21 at 4:30 p.m. Plan on joining in the activities of the Riverboat Jazz Seminar. The fabulous Turkey River All Star Band will entertain us with their festive tunes. Please join us at the Kahler Hotel, Poolside, on Friday, May 21!!!

Special Article

Blinding Hockey Injuries

RICHARD C. HORNS, M.D., M.S. in Ophthalmology*

Forty-seven cases of traumatic eye injuries sustained while playing hockey in Minnesota are reported. There were a variety of mechanisms of injury with stick injuries predominating (66.6%) Injuries most commonly occurred in the ten to fifteen year old group. There was a variety of injuries sustained, and seven (14.6%) resulted in legally blind eyes. Minnesota Statute concerning protective eye wear for school children is discussed.

HOCKEY IS AN INCREASINGLY popular sport among youths in the United States. While it is well known that the frequency of injuries sustained in hockey is high compared to many other sports, the variety of possible injuries is not generally appreciated. Traumatic injury to the eye in hockey has been recognized[1] but is not a common concern as evidenced by the lack of adequate equipment for protection of the eye. It is the intention of this report to document the occurrence of traumatic eye injury in hockey so that the necessity of wearing proper protective equipment will be recognized.

Methods and Results

A survey form developed by the Committee on Ophthalmology of the Minnesota State Medical Assocation (Figure 1) was sent to all members of the Association in 1974. Some cases of serious eye injury were collected before the survey form was sent out, and these cases are included in this report. At the May 1975 meeting of the Committee on Ophthalmology 47 cases of eye injury due to ice hockey and one case of eye injury due to school floor hockey were recorded (Table 1).

The mechanism by which these eyes were in-

TABLE 1

Type	Number of Cases	
I Retinal and Choroidal Injury	11 cases	8 cases with renal or choroidal rupture, or both. 3 cases with retinal and choroidal injury resulting in blindness. 5 cases of retinal detachment requiring surgery resulting in vision of 20/40 or better. 3 cases of macular edema.
II Globe Laceration or Rupture of the Globe	3 cases	All these eyes resulted in blindness.
III Optic Nerve Injury	1 case	This injury resulted in blindness.
IV Orbital Fracture	4 cases	One of these cases developed a traumatic cataract. One of these cases had hyphema Two of these cases were in goalies wearing a conventional goalie mask.
V Hyphema	9 cases	This does not include the two cases of hyphema which also had orbital fractures.
VI Lid and Brow Laceration	15 cases	
VII Miscellaneous	5 cases	1 lid abrasion 1 corneal abrasion 1 subconjunctival hemorrhage 1 iridoplegia 1 zygomatic fracture in a spectator in the stands hit with a puck at a professional hockey game,

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*Clinical Associate Professor, Department of Ophthalmology, University of Minnesota Medical School, Minneapolis, Minnesota.

Address reprint requests to: Richard C. Horns, M.D., 822 Marquette Avenue, Minneapolis, Mn. 55402.

Special Request of the Committee on Ophthalmology
Minnesota State Medical Association

Send Report To:
Committee on Ophthalmology
Minnesota State Medical Association
101 E. 5th St. #900
St. Paul, MN 55101

1. **Name or initials of patient and age of patient:**
2. **City or county where patient resides:**
3. **Physician caring for the patient:**
4. **Mechanism of injury, hockey stick, puck, etc., and approximate date injury occurred:**
5. **Nature and extent of injury; hyphema, corneal laceration, detached retina, etc.:**
6. **Ultimate outcome of injury indicating degree loss of visual function and treatment required:**

Figure 1

jured consisted of 32 cases of eye injury due to being hit with the hockey stick and 12 cases of injury due to being hit with the puck. One case of eye injury was due to the eye being cut with a skate blade, and there was no record of the mechanism of injury in three cases. Although the greatest number of eyes were injured by being hit with the hockey stick, the eyes hit with the hockey puck were generally more severely injured. There were seven blind eyes in the series, and in this group three were blinded by stick injury, three by puck injury, and one by a skate injury.

A high percentage of these injuries were in the school age group (Table 2), and, although information regarding the occurrence of injuries during organized school hockey was not requested, a number of these injuries did occur during hockey play as part of school athletic programs.

TABLE 2
Age Distribution

Under 10 years	4 cases
10 to 15 years	17 cases
16 to 20 years	13 cases
21 years and over	3 cases
Age not reported	11 cases

Case Reports

There were seven eyes which were blinded. A short discussion of these cases follows:

Case 1

This patient, a 15-year-old boy, was hit in the left eye with a hockey puck from a slap shot. The globe was ruptured with complete disorganization of the contents of the globe and with loss of some inner structures of the globe. This injury occurred November 19, 1971. The eye was enucleated.

Case 2

A 14-year-old boy was struck in one eye with a hockey stick. He received a hyphema, retrobulbar hemorrhage, and lid laceration. Traumatic cataract and extensive optic atrophy developed. The resultant vision was light perception with poor light projection. The injury occurred February 4, 1972.

Case 3

This 16-year-old boy was hit in the eye with a puck from a slap shot. The globe received an extensive laceration with loss of the lens and some vitreous at the time of the injury. There was complete disorganization of the remaining contents of the globe with massive intraocular hemorrhage. The globe was retained with bare light perception. This injury occurred in 1973.

Case 4

This 13-year-old boy was struck in the eye with a hockey stick while taking part in floor hockey in a school gymnasium. He received a choroidal tear through the macular area along with hyphema. Following treatment his visual acuity was 20/800 after complete healing. This accident occurred November 8, 1974.

Case 5

A 19-year-old boy was hit in the eye with a hockey stick. He received a traumatic cataract and a detached retina. This eye had complete loss of vision on completion of treatment. The injury occurred in 1974.

Case 6

A nine-year-old boy fell on the ice and was cut across one eye with the blade of a skate. Much of the content of the globe was lost at the time of the injury due to extensive laceration of the globe. This eye was enucleated. The injury occurred in 1974.

Case 7

This patient, a 19-year-old boy, was hit in the eye with a puck from a slap shot. He received a choroidal rupture through the macular area with a submacular hemorrhage. When this eye healed following treatment the vision was 20/200 due to extensive central chorioretinal disorganization. The injury occurred in 1974.

In addition to these blinded eyes there are many eyes in this series with reduced vision which carry the potential for future eye problems due to such conditions as detached retina, traumatic cataract, and secondary glaucoma.

Discussion

Hockey is a sport which has increased in popularity greatly in recent years, and the number of participants continues to increase. The Amateur Hockey Association of the United States states that in 1968-69 there were 3,802 youth teams playing hockey, in 1972-73 there were 9,112 youth teams playing hockey, and in 1974-75 there were 10,844 youth teams playing hockey.[2] It is estimated that in 1975-76 there will be about 75,000 children playing hockey in Minnesota.[3] Girls are becoming interested in hockey and are now playing in competition. In 1974-75 there were 111 girls' teams registered with the Amateur Hockey Association of the United States.[2]

Along with the popularity of hockey, the number of injuries has grown, and eye involvement in hockey injuries is reported to range from one percent[4] to nine percent.[5] The findings described in this report of forty-eight cases of eye injuries due to hockey which occurred in Minnesota are consistent with those of Pashby et al. who, in a similar survey of Canadian Ophthalmologists, reported the occurrence of 287 cases of hockey related eye injuries during 1972-73 and 253 during the following year.[6] In both surveys sticks were found to be the most common cause of injury, accounting for 66.6% of injuries in this series and 60-75% in that of Pashby, and pucks were the second most common cause of injury in both studies. The age distribution of hockey related injuries revealed that the greatest number of those cases in which the age of the player was reported (77%) occurred in the ten to fifteen year old group (45.9%). The Canadian group found a similar distribution. The multiplicity of types of injuries sustained is also similar in both groups. 14.6% of the eye injuries sustained resulted in a legally blind eye. The Canadian group found that 13.7% of those for whom visual acuity was subsequently reported were legally blind in the injured eye.

Although precise figures are not available, it is known that a number of these eye injuries occurred during participation in the athletic programs of public and private schools. The findings of this report are suggestive that participation in school hockey places the student in an area that is potentially hazardous to the eye. By statute of the State of Minnesota it is mandatory that a quality eye protective device be worn when a student is in an area potentially hazardous to the eye (Figure 2). Several helmets with visors and other face protective devices specifically for hockey are being developed.[5]

MINNESOTA SCHOOL EYE SAFETY LAW

126.20 EYE PROTECTIVE DEVICES, Subd. 1. Every person shall wear industrial quality eye protective devices when participating in, observing or performing any function in connection with, any courses or activities taking place in eye protection areas, as defined in Subd. 3, of any school, college, university or other educational institution in the state.

Subd. 2. Any student failing to comply with such requirements may be temporarily suspended from participation in said course and the registration of a student for such course may be cancelled for willful, flagrant or repeated failure to observe the above requirements.

Subd. 3. Eye protection areas shall include, but not be limited to, vocational or industrial arts shops, science or other school laboratories, or school or institutional facilities in which activities are taking place and materials are being used involving:

(a) Hot molten metals;
(b) Milling, sawing, turning, shaping, cutting, grinding or stamping of any solid materials;
(c) Heat treatment, tempering or kiln, firing of any metal or other materials;
(d) Gas or electric arc welding;
(e) Repair or servicing of any vehicle or mechanical equipment;
(f) Any other activity or operation involving work in any area that is potentially hazardous to the eye.

Subd. 4. The governing body of a public educational institution referred to in Subd. 1, may purchase such devices in large quantities for the use of the pupils, teachers and visitors.

Subd. 5. Any person desiring protective-corrective lenses instead of the protective devices supplied by the educational institution shall, at his own expense, procure and equip himself with industrial quality eye protective devices.

Subd. 6. "Industrial quality eye protective devices", as used in this section, shall mean devices meeting the standard of the American Standard Safety Code of Head, Eye and Respiratory Protection, currently identified as: ASA Z2.1-1959.

(Ex1967c14s1subd1-6)

Figure 2

It is the recommendation of the Committee on Ophthalmology of the Minnesota State Medical Association that persons playing hockey wear an eye protective device. In particular, it is the feeling of the Committee that Minnesota statute should require all students taking part in school hockey programs to wear an eye protective device.

The Committee on Ophthalmology also recommends that all youths participating in hockey programs have an evaluation of visual acuity and that anyone who is essentially monocular with marked reduction of vision in one eye be strongly advised not to participate in hockey.

The Committee on Ophthalmology of the Minnesota State Medical Association wishes to express its appreciation to those who responded to the questionnaire. We request that members continue to report cases of hockey eye injuries. Request forms will be sent out again this year.

1. Chilsohm L, Crawford J. Pashby R et al.: Letter: Eye injuries in hockey. Can Med Assoc J 111:501, 1974.
2. 1975 Official Guide, Amateur Hockey Association of the United States.
3. Amateur Hockey Association of the United States: Personal communication, 1975.
4. Marchant L, Roy E Warshawski Jr: Sport Safety Research, 1973-74, UBC school of phys educ for fitness amateur sport branch. Dept Natl Health & Welfare (Can), 1974.
5. Toogood T, Love WB: Hockey injury survey. Can Assoc Health Phys Educ Rec J 32:20, Dec, 1965-Jan, 1966.
6. Pashby TJ, Pashby RC, Chisholm LDJ et al.: Eye injuries in Canadian Hockey. Can Med Assoc J 113:663, 1975.

A.M.A. President, Dr. Max H. Parrott will be there . . . Minnesota Physician and Educator, Dr. Robert W. tenBensel will be there . . . Acting Director of the Federal Bureau of Health Planning & Resources Development, Mr. Eugene J. Rubel will be there . . . May we count on you? C.M.E. '76, May 20-21, Rochester.

Continuing Medical Education

Minnesota Urological Society

Spring Seminar will be held April 10 at the L'hotel Sofitel. Contact: William Price, M.D., 402 Metropolitan Medical Office Building, Minneapolis 55404.

Minnesota Academy of Family Practice

Spring Refresher, April 21 and 22, Radisson South Hotel, Bloomington.

Children's Health Symposium

Fourth Annual Children's Health Center Symposium for Family Physicians, April 23, Children's Health Center, Minneapolis.

University of Minnesota

April 1-3. Allergy and Immunology, Nolte Center for Continuing Education, University of Minnesota Campus, Fee: $100.

April 9-10, Human Aging II, Mayo Memorial Auditorium, University of Minnesota Campus, Fee $15.00.

April 8-10, Practical Dermatology in Primary Care. Nolte Center, University of Minnesota Campus, Fee $100.

Contact: Office of Continuing Medical Education, Box 293, Mayo Memorial Building, Minneapolis, Mn. 55455.

Children's Hospital—St. Paul

Pediatric Conferences; 8:30-9:30 a.m., Auditorium of Hospital:
April 8, Myocarditis and Myocardial Fibroelastosis—Russell Lucas, M.D.
April 22. Study of Theophylline Levels in Asthmatic Children—Edward L. Strem, M.D.

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The nine regional meetings, multidisciplinary in approach, are of interest to a variety of medical specialists and physicians in primary care. Scheduled on weekends, they make it easier and more convenient for you to continue your education. Then there are the two AMA conventions. The Annual *alone* features 53 postgraduate courses, 41 3-hour symposia, the new telecourses and many, many other features in continuing education.

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REGIONAL C.M.E. MEETINGS

Jan. 17, 18	Tulsa, Okla.
Feb. 28, 29	Denver, Colo.
March 17-20	Lexington, Ky.
April 3, 4	Indianapolis, Ind.
April 3, 4	Detroit, Mich.
May 9	Dallas, Tex.
Sept. 4, 5	Jackson Hole, Wyo.
Sept. 11, 12	Milwaukee, Wis.
Sept. 10-12	Portsmouth, N.H.

125th ANNUAL CONVENTION

June 26-30	Dallas, Tex.

30th CLINICAL CONVENTION

Dec. 4-7	Philadelphia, Pa.

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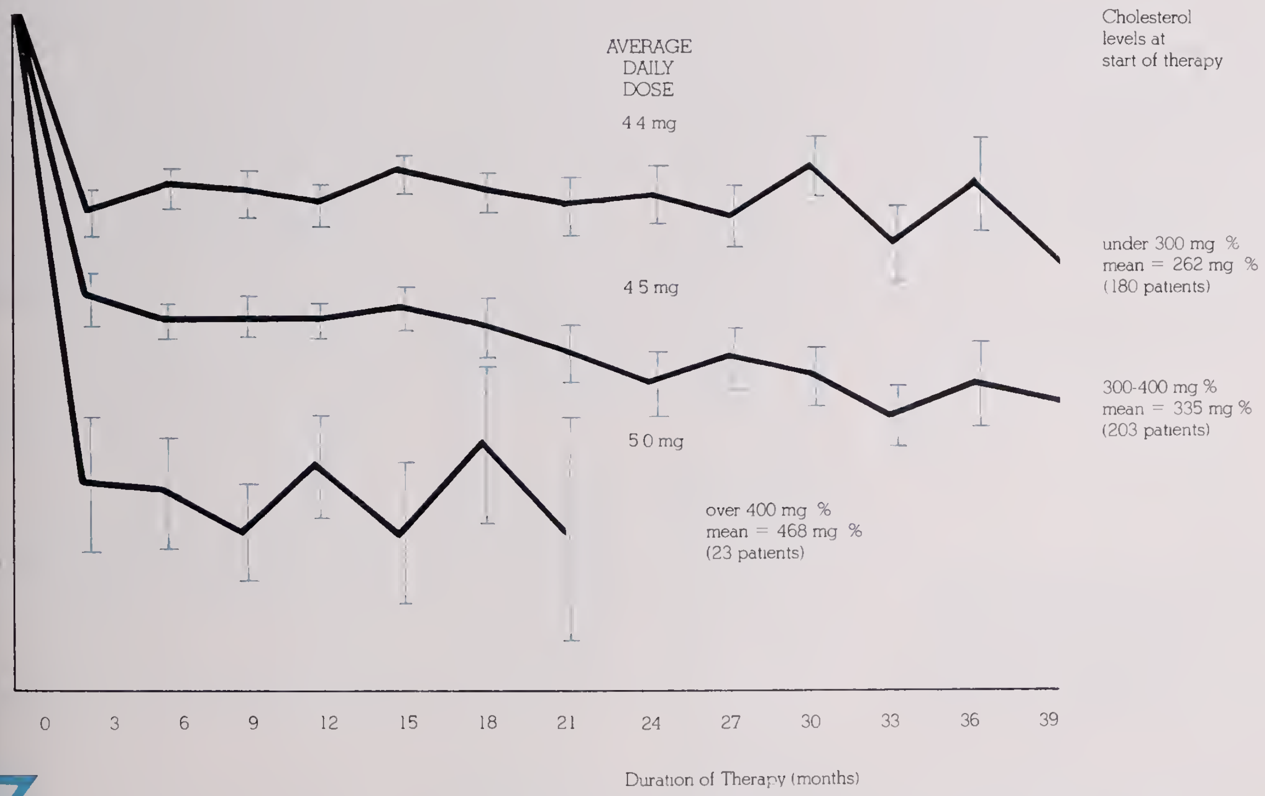
CHOLOXIN (Sodium Dextrothyroxine) is a thyroid analogue which effectively lowers elevated serum cholesterol 15 to 35% (see chart below) in low density lipoproteins.

CHOLOXIN (Sodium Dextrothyroxine) has undergone ten years of clinical trials and seven years of practice. The clinical trials consisted of 337 clinical studies involving over 3,000 hypercholesterolemic non-cardiac patients. It is among the most thoroughly evaluated drugs ever presented to physicians.



NOT ALL PATIENTS ARE REPRESENTED AT EACH TIME INTERVAL

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NOTE:
See following page for full prescribing information.

Choloxin

(Sodium Dextrothyroxine)

Effectively Lowers Elevated Cholesterol With Convenient Once-A-Day Dosage

Four strengths 1, 2, 4, and 6 mg are available making the scored tablet regimen a flexible dosage system. And, for most patients. CHOLOXIN tablets offer once-a-day dosage.

CHOLOXIN* (sodium dextrothyroxine) Single-Tablet-A-Day Dosage Schedules

See prescribing information in package insert reproduced below

	Starting Dosage	Increased Monthly by	Usual Maintenance	Maximal Recommende
Adult Hypercholesterolemic	1 0-2 0 mg	1 0-2 0 mg	4 0-8 0 mg	4 0-8 0 mg
Pediatric Hypercholesterolemic	0 05 mg /kg body weight	0 05 mg /kg	0 1 mg /kg body weight	4 0 mg
Hypothyroid Cardiac	0 5-1 0 mg	1 0 mg	4 0 mg	4 0 mg

Description

CHOLOXIN (sodium dextrothyroxine) is the sodium salt of the dextrorotatory isomer of thyroxine It is chemically described,as D-3 5,3' 5'-tetraiodothyronine sodium salt

Actions

The predominant effect of CHOLOXIN (sodium dextrothyroxine) is the reduction of serum cholesterol levels in hyperlipidemic patients Beta lipoprotein and triglyceride fractions may also be reduced from previously elevated levels

Most of the available evidence indicates that CHOLOXIN stimulates the liver to increase catabolism and excretion of cholesterol and its degradation products via the biliary route into the feces Cholesterol synthesis is not inhibited and abnormal metabolic end products do not accumulate in the blood

Indications

This is not an innocuous drug Strict attention should be paid to the indications and contraindications.

CHOLOXIN (sodium dextrothyroxine) is an antilipidemic agent used as an adjunct to diet and other measures for the reduction of elevated serum cholesterol (low density lipoproteins) in euthyroid patients with no known evidence of organic heart disease

The drug is also indicated in the treatment of hypothyroidism in patients with cardiac disease who cannot tolerate other types of thyroid medication **Before prescribing, note the following Results from a randomized clinical study have indicated a possible adverse effect when CHOLOXIN (sodium dextrothyroxine) is administered to a patient receiving a digitalis preparation There may be an additive effect This additive effect may possibly stimulate the myocardium excessively in patients with significant myocardial impairment CHOLOXIN (sodium dextrothyroxine) dosage should not exceed 4 mg per day when the patient is receiving a digitalis preparation concomitantly Careful monitoring of the total effect of both drugs is important.**

It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question

Contraindications

The administration of CHOLOXIN sodium dextrothyroxine to euthyroid patients with one or more of the following conditions is contraindicated

1 Known organic heart disease including angina pectoris history of myocardial infarction cardiac arrhythmia or tachycardia either active or in patients with demonstrated propensity for arrhythmias rheumatic heart disease history of congestive heart failure and decompensated or borderline compensated cardiac status
2 Hypertensive states (other than mild labile systolic hypertension
3 Advanced liver or kidney disease
4 Pregnancy
5 Nursing mothers
6 History of iodism

Warnings

CHOLOXIN (sodium dextrothyroxine) may potentiate the effects of anticoagulants on prothrombin time. Reductions of anticoagulant dosage by as much as 30% have been required in some patients Consequently, the dosage of anticoagulants should be reduced by one-third upon initiation of CHOLOXIN (sodium dextrothyroxine) therapy and the dosage subsequently readjusted on the basis of prothrombin time. The prothrombin time of patients receiving anticoagulant therapy concomitantly with CHOLOXIN (sodium dextrothyroxine) therapy should be observed as frequently as necessary, but at least weekly, during the first few weeks of treatment

In the surgical patient it is wise to consider withdrawal of the drug two weeks prior to surgery if the use of anticoagulants during surgery is contemplated

When CHOLOXIN (sodium dextrothyroxine is used as thyroid replacement therapy in hypothyroid patients with concomitant coronary artery disease (especially those with a history of angina pectoris or myocardial infarction) or other cardiac disease treatment should be initiated with care Special consideration of the dosage schedule of CHOLOXIN (sodium dextrothyroxine is required This drug may increase the oxygen requirements of the myocardium especially at high dosage levels Treated subjects with coronary artery disease must be seen at frequent intervals If aggravation of angina or increased myocardial ischemia cardiac failure or clinically significant arrhythmia develops during the treatment of hypothyroid patients the dosage should be reduced or the drug discontinued

Special consideration must be given to the dosage of other thyroid medications used concomitantly with CHOLOXIN (sodium dextrothyroxine) As with all thyroactive drugs hypothyroid patients are more sensitive to a given dose of CHOLOXIN (sodium dextrothyroxine) than euthyroid patients

Epinephrine injection in patients with coronary artery disease may precipitate an episode of coronary insufficiency This condition may be enhanced in patients receiving thyroid analogues These phenomena should be kept in mind when catecholamine injections are required in sodium dextrothyroxine-treated patients with coronary artery disease

Since the possibility of precipitating cardiac arrhythmias during surgery may be greater in patients treated with thyroid hormones it may be wise to discontinue CHOLOXIN (sodium dextrothyroxine) in euthyroid patients at least two weeks prior to an elective operation During emergency surgery in euthyroid patients and in surgery in hypothyroid patients in whom it may not be advisable or possible to withdraw therapy the patients should be carefully observed

There are reports that sodium dextrothyroxine in diabetic patients is capable of increasing blood sugar levels with a resultant increase in requirements of insulin or oral hypoglycemic agents Special attention should be paid to parameters necessary for good control of the diabetic state in dextrothyroxine-treated subjects and to dosage requirements of insulin or other antidiabetic drugs If sodium dextrothyroxine is later withdrawn from patients who required an increase of insulin or oral hypoglycemic agents dosage during its administration the dosage of antidiabetic drugs should be reduced and adjusted to maintain good control of the diabetic state

When either or both impaired liver or kidney function are present the advantages of CHOLOXIN (sodium dextrothyroxine) therapy must be weighed against the possibility of deleterious results

Usage in Women of Childbearing Age

Women of childbearing age with familial hypercholesterolemia or hyperlipemia should not be deprived of the use of this drug it can be given to those patients exercising strict birth control procedures Since pregnancy may occur despite the use of birth control procedures administration of CHOLOXIN (sodium dextrothyroxine) to women of this age group should be undertaken only after weighing the possible risk to the fetus against the possible benefits to the mother Teratogenic studies in two animal species have resulted in no abnormalities in the offspring

Precautions

It is expected that patients on dextrothyroxine therapy will show greatly increased serum protein-bound iodine levels These increased serum PBI values are evidence of absorption and transport of the drug and should NOT be interpreted as evidence of hypermetabolism similarly they may not be used for titrating the effective dose of CHOLOXIN (sodium dextrothyroxine PBI values in the range of 10 to 25 mcg% in treated patients are common

If signs or symptoms of iodism develop during CHOLOXIN sodium dextrothyroxine therapy the drug should be discontinued

A few children with familial hypercholesterolemia have been treated with CHOLOXIN (sodium dextrothyroxine for periods of one year or longer with no adverse effects on growth However it is recommended that the drug be continued in patients in this age group only if a significant serum cholesterol lowering effect is observed

Adverse Reactions

The side effects attributed to dextrothyroxine therapy are for the most part due to increased metabolism and may be minimized by following the recommended dosage schedule Adverse effects are least commonly seen in euthyroid patients with no signs or symptoms of organic heart disease the incidence of adverse effects is increased in hypothyroid patients and is highest in those patients with organic heart disease superimposed on the hypothyroid state

In the absence of known organic heart disease some cardiac changes may be precipitated during sodium dextrothyroxine therapy In addition to angina pectoris arrhythmia consisting of extrasystoles ectopic beats or supraventricular tachycardia ECG evidence of ischemic myocardial changes and increase in heart size have been observed Myocardial infarctions both fatal and non fatal have occurred but these are not unexpected in untreated patients in the age groups studied It is not known whether any of these infarcts were drug related

Changes in clinical status that may be related to the metabolic action of the drug include the development of insomnia nervousness palpitations tremors loss of weight lid lag sweating flushing hyperthermia hair loss diuresis and menstrual irregularities Gastrointestinal complaints during therapy have included dyspepsia nausea and vomiting constipation diarrhea and decrease in appetite

Other side effects reported to be associated with CHOLOXIN (sodium dextrothyroxine) therapy include the development of headache changes in libido (increase or decrease) hoarseness tinnitus dizziness, peripheral edema malaise tiredness visual disturbances psychic changes paresthesia muscle pain and various bizarre subjective complaints Skin rashes including a few which appeared to be due to iodism and itching have been attributed to dextrothyroxine by some investigators Gallstones have been discovered in occasional dextrothyroxine-treated patients and cholestatic jaundice has occurred in one patient although its relationship to CHOLOXIN (sodium dextrothyroxine) therapy was not established

In several instances the previously existing conditions of the patient appeared to continue or progress during the administration of CHOLOXIN (sodium dextrothyroxine) a worsening of peripheral vascular disease sensorium exophthalmos and retinopathy have been reported

CHOLOXIN (sodium dextrothyroxine) potentiates the effects of anticoagulants such as warfarin or Dicumarol on prothrombin time thus indicating a decrease in the dosage requirements of the anticoagulants On the other hand dosage requirements of antidiabetic drugs have been reported to be increased during dextrothyroxine therapy (see WARNINGS section)

Dosage and Administration

For **adult** euthyroid hypercholesterolemic patients the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is 4 to 8 mg per day The initial daily dose should be 1 to 2 mg to be increased in 1 to 2 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily if that dosage level is indicated to effect the desired lowering of serum cholesterol

When used as partial or complete substitution therapy for levothyroxine in hypothyroid patients with cardiac disease who cannot tolerate other types of thyroid medication the initial daily dose should be 1 mg to be increased in 1 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily preferably the lower dosage The maximum in patients receiving digitalis therapy is 4 mg

For **pediatric** hypercholesterolemic patients the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is approximately 0 1 mg (100 mcg) per kilogram The initial daily dosage should be approximately 0 05 mg (50 mcg) per kilogram to be increased in up to 0 05 mg (50 mcg) per kilogram increments at monthly intervals The recommended maximal dose is 4 mg daily if that dosage is indicated to effect the desired lowering of serum cholesterol

If new signs or symptoms of cardiac disease develop during the treatment period the drug should be withdrawn

How Supplied

CHOLOXIN (sodium dextrothyroxine) is supplied in prescription packages of scored 1 2 4 and 6 mg tablets

March 1975

FLINT LABORATORIES
DIVISION OF TRAVENOL LABORATORIES, INC.
Deerfield, Illinois 60015

Minnesota Department of Health

Hepatitis-B Surface Antigen among Residents of An Institution for the Mentally Retarded

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and ROBERT A. SIEM, PH.D.#

Fifty-five (7.6 percent) of 728 residents of an institution for the mentally retarded were found to have serum positive for hepatitis-B surface antigen (HB$_s$Ag), and 23 residents (3.2 percent) were found positive for hepatitis-B surface antibody (anti-HB$_s$). All but six remained antigenemic on repeated examinations. Rates of antigenemia were highest among those with Down syndrome, males, teen-agers, those institutionalized before age 10, those at the institution for 5-9 years, and non-toilet-trained, ambulatory individuals. The last of these associations suggests the possibility of non-parenteral transmission of hepatitis-B virus. Approximately two-thirds of the antigenemic individuals had persistently abnormal serum transaminase levels. Further studies at this institution will attempt to delineate high-risk groups more explicitly and explain better the potential mechanisms of transmission.

THE PREVALENCE AND transmission of hepatitis-B virus have been the subjects of numerous studies in many different population groups throughout the world.[1,2] Since 1967, when a high prevalence of Australian antigen carriers was reported among Down syndrome patients,[3] many investigations focused on residents of institutions for the mentally retarded, who, for reasons not completely understood, have a higher prevalence of antigenemia than the general population.[4-11]

This report, which reviews preliminary findings of a continuing study at a large institution for the mentally retarded in Minnesota, further describes the dimensions of this problem.

Faribault State Hospital, in southeastern Minnesota, has approximately 1200 residents,§ varying in age from five to 92 years and with a slight preponderance of males (56 percent). Between 1971 and 1974, it had 980 to 1210 employees. Residents have various degrees of mental retardation due to many different etiologies. About one-sixth have Down syndrome. Because of the suspected high prevalence of antigenemia among residents there, the institution in cooperation with the Minnesota Department of Health began in November 1970 a study of antigenemia among them.

Methods

Serum was obtained from 728 (49 percent) residents between November 1970 and March 1974, and tested for HB$_s$Ag by counterelectrophoresis and complement fixation tests, and for hepatitis-B surface antibody (anti-HB$_s$) by counterelectrophoresis at the Division of Medical Laboratories, Minnesota Department of Health.[12-16] For the most part, residents of 27 dormitories were selected by stratified random sampling. However, eventually a somewhat greater proportion of individuals screened were residents of dormitories that had a higher incidence of antigenemia than others. Many of the individuals were tested

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§Based on 1974 resident census. In late 1970, at the start of the study, the resident census was approximately 1500.

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more than once during the course of the study, but only the first test result for each individual is considered in this report.

The following data were abstracted from institution records for each individual tested: age; sex; building of residence; age and year of admission; functional level at time of test (relating to ambulation and eating and toilet habits); and type, cause, and severity of mental retardation. Data were hand tabulated and analyzed primarily by applying chi-square tests to 2x2 contingency tables. Serum glutamic oxaloacetic transaminase (SGOT) and glutamic pyruvic transaminase (SGPT) levels were obtained from most antigenemic individuals in 1972 and again in 1973.

The medical director of the hospital obtained from hospital records the number of acute viral hepatitis cases clinically diagnosed in residents and employees of the institution between 1971 and 1974.

Results

Of the 728 individuals tested, 55 (7.6 percent) had serum positive for HB$_s$Ag. All but six remained positive on repeated tests from 1971 to 1974.

Antigenemia was statistically significantly more frequent among those with Down syndrome (Table 1). Most of the 24 HB$_s$Ag-positive individuals without Down syndrome had mental retardation apparently due to a congenital anomaly, although often such an anomaly was not specified in an individual's medical record. Only four of these individuals were mentally retarded because of birth injury or postnatal events.

TABLE 1
Rate of Antigenemia by Presence of Down Syndrome

Disease Status	HB$_s$Ag-Positive	HB$_s$Ag-Negative	Percent Positive*
Down Syndrome	31	97	24.2
No Down Syndrome	24	576	4.0
TOTAL	55	673	7.6

*χ^2=58.88, $p < .001$

A statistically significantly higher percentage of males than females was antigenemic; this sex difference was most significant among those without Down syndrome (Table 2). Analysis of data by age revealed that the highest rate of antigenemia was among teen-agers (Table 3). Persons under age 20 years had a significantly higher rate of antigenemia (11.9 percent) than those 20 years of age and older (3.5 percent) ($p < .001$). All eight antigenemic females were under age 20.

TABLE 2
Rate of Antigenemia by Sex and Presence of Down Syndrome

Patient Category	HB$_s$Ag-Positive	HB$_s$Ag-Negative	Percent Positive
All Males	47	357	11.6*
All Females	8	316	2.5
Down Males	24	52	31.6†
Down Females	7	45	13.5
Non-Down Males	23	305	7.0‡
Non-Down Females	1	271	0.4

*χ^2=20.32, $p < .001$
†χ^2=4.57, $p < .05$
‡χ^2=15.40, $p < .001$

Analysis of the data by functional level and mobility revealed that the highest rates of antigenemia were among non-toilet-trained, ambulatory individuals* (Table 4). Among the ambulatory individuals, those who were not toilet-trained (functional levels B and C) had a significantly

TABLE 3
Rate of Antigenemia by Age at Test and Sex

Age at Test (in Years)		HB$_s$Ag-Positive	HB$_s$Ag-Negative	Percent Positive*
Males:	0-9	3	29	9.4
	10-19	31	143	17.8
	20-29	10	74	11.9
	30-39	1	65	1.5
	40-49	2	29	6.5
	50 +	0	17	0.0
Females:	0-9	1	26	3.7
	10-19	7	112	5.9
	20-29	0	77	0.0
	30-39	0	39	0.0
	40-49	0	30	0.0
	50 +	0	32	0.0

*When the rate for all males and females age 19 years and younger is compared with the rate for all those age 20 years and older, χ^2=17.50 and $p < .001$.

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*All residents not fully toilet-trained were considered non-toilet-trained, and all those not fully ambulatory were considered non-ambulatory.

higher rate of antigenemia (13.7 percent) than those who were toilet-trained (functional level A, 7.2 percent). Among the non-toilet-trained individuals, those who were ambulatory (functional levels B and C) had a significantly higher rate of antigenemia (13.7 percent) than those who were non-ambulatory (functional level D, 1.4 percent). Antigenemia was more strongly associated with ambulation than with lack of toilet training.

Those admitted at age nine years or younger had significantly higher rates of antigenemia than those admitted at a later age (Table 5). Those admitted in the 1960-1964 and 1965-1969 periods had higher rates of antigenemia than those admitted in other periods (Table 6). (The median test ages of those admitted in 1960-1964 was approximately 13, and, in 1965-1969, approximately 17 years.) Those present at the institution five to nine years had a significantly higher rate of antigenemia than all those present for shorter and longer periods (Table 7).

Forty-six of the 47 antigenemic males lived in 11 all-male buildings with from one to 17 antigenemic residents and rates of antigenemia ranging from five to 60 percent. There was a trend of clustering of antigenemia in all-male buildings with relatively low median ages, but the small number of all-male buildings precluded the dem-

TABLE 4
Antigenemia by Functional Level and Mobility

Functional Level	Definition of Functional Level: Ambulatory	Toilet-Trained	Eat with Assistance	HB_sAg-Positive	HB_sAg-Negative	Percent Positive	
A	yes	yes	no	29	377	7.2	
B	yes	no	no	17	87	16.4	*
C	yes	no	yes	7	64	9.9	†
D	no	no	yes	2	145	1.4	

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*When combined data for functional levels B and C are compared with data for level A, $\chi^2=5.60$ and $p < .02$.

†When combined data for functional levels B and C are compared with data for level D, $\chi^2=14.80$ and $p < .001$.

TABLE 5
Antigenemia by Admission Age

Admission Age (in Years)	HB_sAg-Positive	HB_sAg-Negative	Percent Positive*
0-4	15	93	13.9
5-9	28	222	11.2
10-14	8	153	5.0
15-19	2	98	2.0
20-24	0	45	0.0
25 +	2	62	3.1

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*When the rate for those admitted at age 9 years or younger is compared with the rate for those admitted at age 10 or older, $\chi^2=18.79$ and $p < .001$.

TABLE 6
Antigenemia by Year Admitted

Year Admitted	HB_sAg-Positive	HB_sAg-Negative	Percent Positive*
Before 1960	10	270	3.6
1960-1964	25	141	15.1
1965-1969	17	113	13.1
1970-1973	3	149	2.4

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*When the rate for all those admitted in the 1960-1964 and 1965-1969 periods is compared with the rate for all those admitted before 1960 and in the 1970-1973 period, $\chi^2=33.05$ and $p < .001$.

TABLE 7
Antigenemia by Number of Years Present at Institution

Number of Years Present	HB_sAg-Positive	HB_sAg-Negative	Percent Positive*
0-4	14	201	6.5
5-9	17	123	12.1
10 +	24	349	6.4

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*When the rate for those present at the institution 5-9 years is compared with the rate for all those present 0-4 and 10 or more years, $\chi^2=4.44$ and $p < .05$.

onstration of any strong statistical association between these two variables.

Twenty-three (3.2 percent) of the 728 individuals tested in this survey (16 males and seven females) were positive for anti-HB_s.

None of the 55 individuals who were found to be HB_sAg positive during this survey had clinically recognized acute viral hepatitis. Between 1971 and 1974, there were six cases of acute hepatitis-B clinically diagnosed among hospital residents and eight among employees. During this period, there were no cases of hepatitis-A clinically diagnosed among hospital residents and three among employees.

SGOT and SGPT determinations performed twice on 31 of these antigenemic individuals, first in September-October 1972 (a median time of 16 months after they were first noted to be antigenemic) and again in February 1973, were within normal limits in approximately one-third, between one and two times the upper limit of normal in approximately one-third, and above two times normal in the remaining one-third. There was little change in these parameters of liver function between first and second times of testing: six had slight and one substantial improvement, and two had slight worsening. There was no substantial difference in liver function between those with and those without Down syndrome. Too few antigenemic females were tested to compare liver function in antigenemic males and females.

Discussion

This preliminary report of an ongoing investigation describes the distribution of HB_sAg among residents of a large institution for the mentally retarded. The high-risk groups found in this study have certain characteristics similar to those of other studies on similar populations.

Presence of Down Syndrome

The rate of antigenemia among patients with this syndrome was 24 percent in our study, only slightly lower than the 30 percent average of rates in many other studies, which have confirmed Blumberg's original observation of this association.[3,17] The high prevalence (and prolonged persistence) of antigenemia among Down patients may be due to a genetically-determined immunologic defect or their peculiar mechanism of host response to infections.[17] Available data on immunoglobulin levels in these patients lacks uniformity,[8,17] necessitating further study of this possible mechanism.

Male Sex

The significantly higher rate of antigenemia among males (Table 2) is an intriguing finding not easily explained at present. A male preponderance of similar magnitude has been demonstrated in studies of three large institutions for the mentally retarded,[8,9,11] but in a matched-pair study of a state school, male predominance was demonstrated only among those admitted at age 10 years or older.[10] Interestingly, a male predominance of antigenemia has been reported in some groups of voluntary blood donors, and among "healthy" HB_sAg carriers in Senegal, and among native populations of Peru and Cebu.[2,18,19] Genetic, immunologic, hormonal, and other differences between the sexes have been postulated as possible explanations. Another explanation might be the patterns of behavior and interaction among males at this institution. Further investigation is necessary.

Age-Related Risk Factors

Our findings that the rate of antigenemia was highest among teen-agers (Table 3), among those admitted to the institution at age nine years or younger (Table 5), and among those residing at the institution for five to nine years (Table 7) are in agreement with those of other studies on similar populations.[8-11]

Functional Level and Mobility

The higher rate of antigenemia in our study among *non-toilet-trained, ambulatory* individuals (Table 4), a finding not previously reported, demonstrates that ambulation, with its associated increased interpersonal interaction, plays an important role in the spread of hepatitis-B virus infection. It also strongly suggests the possibility of non-parenteral transmission of hepatitis-B virus in this population. Szmuness and co-workers did not find a difference in antigenemia rates between ambulant and non-ambulant residents at Wassaic State School, nor a decisive influence of IQ and functional levels on risk of antigenemia.[10] Chance, however, in her report on an antigenemia survey of mentally retarded residents at Sonoma State Hospital, speculated that ambulation might be a high-risk factor.[11]

The exact mode of transmission of hepatitis-B virus among residents at Faribault State Hospital is a matter of speculation. The opportunity for residents of an institution for the mentally retarded to be exposed to human excreta is greater than for the general population. Our data suggest that such exposures are an important factor. Numerous published reports on the presence of HB_sAg in urine, feces, saliva, and semen, and on probable transmission of hepatitis-B by kissing, sexual contact, human bites, and other mechanisms raise issues for further study.[20-29] Similarily, the clustering of antigenemia in certain dormitories in this study, as observed in other studies,[8,10,11] is not easily explained and requires further study.

Persistently abnormal transaminase levels in many antigenemic individuals in our study suggest the possibility of much chronic liver disease among them; this possibility also requires additional investigation. The rate of such abnormalities in this study is similar to the 37 percent of antigenemic mentally retarded individuals in another study who had abnormal transaminase levels, most of which persisted.[8,17]

Although methods we used to test for HB_sAg are no longer considered as the most sensitive ones, there is some indication that in detection of chronic HB_sAg carriers, available methods may differ little in their sensitivity.[30] Although further investigation and analyses on hepatitis-B virus transmission at this institution are necessary, this preliminary report nevertheless describes several interesting findings thus far and directions of future studies.

In view of the low incidence of acute hepatitis-B among close personal contacts of antigenemic residents of this institution, these residents did not represent any substantial risk to others. Further assessment of this matter is necessary, but in the meantime we do not recommend unusually stringent precautions for HB_sAg carriers. Those with responsibility for care of such individuals, however, should practice scrupulous handwashing techniques and consider wearing gloves in certain situations. Also, personal toiletry items should not be shared with them.

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Testing in Humans: Who, Where & When.

The weight of ethical opinion:

Few would disagree that the effectiveness and safety of any therapeutic agent or device must be determined through clinical research.

But now the *practice* of clinical research is under appraisal by Congress, the press and the general public. Who shall administer it? On whom are the products to be tested? Under what circumstances? And how shall results be evaluated and utilized?

The Pharmaceutical Manufacturers Association represents firms that are significantly engaged in the discovery and development of new medicines, medical devices and diagnostic products. Clinical research is essential to their efforts. Consequently, PMA formulated positions which it submitted on July 11, 1975, to the Subcommittee on Health of the Senate Labor and Public Welfare Committee, as its official policy recommendations. Here are the essentials of PMA's current thinking in this vital area.

1. PMA supports the mandate and mission of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and offers to establish a special committee composed of experts of appropriate disciplines familiar with the industry's research methodology to volunteer its service to the Commission.

2. PMA supports the formation of an independent, expert, broadly based and representative panel to assess the current state of drug innovation and the impact upon it of existing laws, regulations and procedures.

3. When FDA proposes regulations, it should prepare and publish in the *Federal Register* a detailed statement assessing the impact of those regulations on drug and device innovation.

4. PMA proposes that an appropriately qualified medical organization be encouraged to undertake a comprehensive study of the optimum roles and responsibilities of the sponsor and physician when company-sponsored clinical research is performed by independent clinical investigators.

5. PMA recognizes that the physician-investigator has, and should have, the ultimate responsibility for deciding the substance and form of the informed consent to be obtained. However, PMA recommends that the sponsor of the experiment aid the investigator in discharging this important responsibility by providing (1) a document detailing the investigator's responsibilities under FDA regulations with regard to patient consent, and (2) a written description of the relevant facts about the investigational item to be studied, in comprehensible lay language.

6. In the case of children, the sponsor must require that informed consent be obtained from a legally appropriate representative of the participant. Voluntary consent of an older child, who may be capable of understanding, in addition to that of a parent, guardian or other legally responsible person, is advisable. Safety of the drug or device shall have been assessed in adult populations prior to use in children.

7. PMA endorses the general principle that, in the case of the mentally infirm, consent should be sought from both an understanding subject and from a parent or guardian, or in their absence, another legally responsible person.

8. Pharmaceutical manufacturers sponsoring investigations in prisons must take all reasonable care to assure that the facilities and personnel used in the conduct of the investigations are suitable for the protection of participants, and for the avoidance of coercion, with a respect for basic humanitarian principles.

9. Sponsors intending to conduct nontherapeutic clinical trials through the participation of employee volunteers should expand the membership and scope of its existing Medical Research Committee, or establish such an internal Medical Research Committee, with responsibility to approve the consent forms of all volunteers, designs, protocols and the scope of the trial. The Committee should also bear responsibility to ensure full compliance with all procedures intended to protect employee volunteers' rights.

10. Where the sponsor obtains medical information or data on individuals, it shall be accorded the same confidential status as provided in codes of ethics governing health care professionals.

11. PMA and its member firms accept responsibility to aid and encourage appropriate follow-up of human subjects who have received investigational products that cause latent toxicity in animals or, during their use in clinical investigation, are found to cause unexpected and serious adverse effects.

12. PMA supports the exploration and development by its member companies of more systematic surveillance procedures for newly marketed products.

13. When a pharmaceutical manufacturer concludes, on the basis of early clinical trials of a basic new agent, that a new drug application is likely to be submitted, a proposed development plan accompanied by a summary of existing data, would be submitted to the FDA. Following a review of this submission, the FDA, and its Advisory Committee where appropriate, would meet with the sponsor to discuss the development plan. No *formal* FDA approval should be required at this stage. Rather, the emphasis should be on identification of potential problems and questions for the sponsor's further study and resolution as the program develops.

The PMA believes that health professionals as well as the public at large should be made aware of these 13 points in its Policy on Clinical Research. For these recommendations envisage constructive, cooperative action by industry, research institutions, the health professions and government to encourage creative and workable responses to issues involved in the clinical investigation of new products.

P·M·A

Pharmaceutical Manufacturers
Association
1155 Fifteenth Street, N.W.
Washington, D. C. 20005

Book Reviews

THE PATHOLOGY OF HOMICIDE, Lester Adelson, M.D., Charles C. Thomas, 976 pages, 1974.

Quis, quid, ubi, quibus, auxilis, cur, quomodo,
quando?
Who, what, where, with what, with whose help, why,
how, and when?
What was the crime, who did it, when was it done
and where?
How done and with what motive; who in the deed
did share?

Author Unknown

Doctor Lester Adelson is perhaps America's best-known forensic pathologist. This fame comes from his skills as a writer and speaker, from his being part of well-known murder trials, and from hard-earned knowledge. For over 20 years, he has labored, observed, recorded, and argued in the morgues and courtrooms of Cleveland's Cuyahoga County.

The book offers insight into the nature of homicide in this country. Here, for example, is a passage from Adelson's introductory chapter:

"The fact that police authorities are powerless to *prevent* a large proportion of these lethal crimes derives from the circumstances and motives surrounding the fatal incident. Unlike other serious criminal offenses (e.g. burglary, robbery and kidnapping), criminal homicide is, to a large extent, an *intimate, personal* crime as demonstrated by the fact that most homicide victims are killed by close relatives, friends and acquaintances.

In addition to being well-written, the book is comprehensive, graphic, and factual. Within its pages you will find described and depicted bludgeoned, stabbed, shot, strangled, incinerated, raped, abused, beaten, aborted, and poisoned victims. And you will run across many tables listing statistics like these:

Homicides in Cuyahoga County, 1951-1972, 3052; Firearms, 2041 (67%); Blunt violence, 330 (11%); Edged or pointed weapons, 559 (18%); Strangulation, 64 (2%); Others, 58 (2%).

And this:

Postmortem blood alcohol levels in deaths in Cuyahoga County, 1958-1971, 38,499 tested for alcohol levels. Homicide: number tested, 1994; percent positive, 58.1%. Vehicular deaths: number tested, 1875; percent positive, 45.0%. Suicide: number tested, 2251; percent positive, 26.2%. Natural causes: number tested 32,379, percent positive, 9.5%.

But perhaps the most useful part of the book, at least for the pathologist inexperienced in forensic matters, are the early chapters on the hows, whys, whens, and whats of establishing the mode, manner, and causes of violent death. Adelson also has a wise concluding chapter on how to act in court as a witness.

Summary: A murderously good book.

Richard C. Reece, M.D.
Editor-in-Chief

PLANNING FOR CARDIAC CARE; A GUIDE TO THE PLANNING AND DESIGN OF CARDIAC CARE FACILITIES by Colin W. Clipson and Joseph J. Wehrer. The Health Administration Press of the University of Michigan, Ann Arbor. 1973, Folio. 407 pages. Paper back.

Clipson and Wehrer of the Department of Architecture, University of Michigan, address themselves to the total problem of the Coronary Care Unit (CCU): how to plan, design, build, staff, and operate the CCU. It answers authoritatively innumerable questions that must arise when a hospital undertakes to initiate or redesign a CCU: how many beds, how many rooms of what size, wiring, plumbing, oxygen, support systems, monitors, crash carts, staffing, administration, nursing, role of the doctors, the works. Intricate (probably too intricate) flow sheets attempt to answer all questions of admission of patients, transfer to the CCU, what to do until the doctor arrives, what the doctor should do thereafter. This must become the classic reference from the standpoint of the architect.

In their attempt to compress everything into 400 pages with about a thousand illustrations the authors have erred by compressing illustrations to such a degree that I found it necessary even with 20/15 vision to read the captions with the aid of a 5D reading glass. The book measures 9 x 12 inches, outsize; the pages are printed in three columns and are legible. The authors probably don't believe in the adage that a picture is worth a thousand words.

Of particular interest to personnel newly assigned to the CCU are the several flow sheets that indicate procedure to follow as the case develops. I suspect such instruction will eventually result in computer programming with the next step in patient care interrogated on a typewriter and answered on a television screen. This work will probably see more editions.

Reuben Berman, M.D.
Editor Emeritus

THE FIRST FIVE YEARS—Virginia Pomeranz, M.D. and Dod. Schultz. Doubleday and Company, Garden City, New York 1973. $6.95.

This book contains much advice, I always intended to write for my patients, but never did. Dr. Pomeranz and Mrs. Schultz have done it well in a comfortable, highly readable style. While addressed primarily to parents, the book is good reading for all persons involved with small child care.

Martha Strickland, M.D.
Uvalde, Texas

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FOR LONG-TERM CONTROL OF HYPERTENSION*

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SPARES POTASSIUM

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

> *Warning
> This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

*Indications: *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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Family Practice

A Flexible and Functional Definition of Family Practice

ROBERT R. THOMPSON, M.D.* and CHARLES G. ROLAND, M.D.†

The terms "primary care," "ambulatory care," and "family practice" can and should be sorted out semantically. Both semantically and functionally, the family practitioner emerges as a distinct species and probably is not on the endangered list. The family practitioner's role is defined functionally as he responds in his postgraduate efforts to his medical environment, social community, and personal preferences. The diagrammatic model we propose shows how a hypothetical family physician integrates portions of the various specialty disciplines in medicine into a functional definition, showing their relation to ambulatory and to inpatient care.

ALTHOUGH COMPLETE and convincing definitions of family medicine and of family practice could serve many useful purposes, there seems little likelihood of arriving at firm definitions that would be widely accepted. Both family medicine (the academic discipline) and family practice are holistic and pervasive entities that defy the dictionary's straightjacket. This is true most particularly of family practice, which each practitioner defines by doing. Certain broad categoric principles can be agreed upon. After that, malleability must be built into any definition; it is this trait that we have attempted to display in our description.

With more than 250 residency programs available, with the number of applicants exceeding the number of positions, and with greatly increased numbers of medical students (the best and the brightest, we are told) seeking family practice experience, it is not surprising that many are asking "What is family practice?"

According to at least one author, the American Academy of Family Practice (AAFP) ". . . has not been able to get across to outsiders precisely what the family physician knows and does that other people don't."[1] Not that the questions haven't been asked and some answers proffered, but these have often been vague, and the unanswered question remains: Is family practice a distinct specialty of medicine whose practitioners possess or aspire to possess some knowledge and skills that other already established medical specialties do not?

Some Current Definitions

The American Academy of Family Practice has offered a definition. If not concise, it is readable, germane, and has served as a useful model. It suggests that the family physician be defined as a physician who practices in the discipline of family practice and whose training and experience qualify him to practice in several fields of medicine and surgery, with particular emphasis on the family unit, and who:

1. Serves the public as the physician of first contact and as the means of entry into the health care system.
2. Evaluates his patient's total health needs, provides personal medical care within one or more fields of medicine, and refers patients when indicated to appropriate sources of care while preserving the continuity of his own care.
3. Develops a responsibility for his patient's comprehensive and continuous health care and acts as coordinator of his patient's health services.
4. Accepts responsibility for his patient's total health care, including the use of consultants, within the context of their environment—the family or comparable social unit and the community.[2]

Relating that definition of a family practitioner to primary medicine, Alpert and Charney[3] suggest, in a recent monograph, that family medicine is a subset of primary medicine, both of which subserve the criteria of first contact with the patient, longitudinal responsibility, and a broad integrationist role. They point out that broadness of responsibility rather than broadness of vision delineates the "consultant" from the primary physician. Thus, however compassionate and however great his psychologic orientation, the average subspecialist's main professional concern is with an afflicted organ or system and he is ill-equipped and ill-advised to assume the integrationist function or to assume responsibility for the management of the patient's psychosocial problems.

A moot point is the ideal role of the general internist in providing primary care. Obviously, many internists are functioning as primary care physicians. Whether this is an appropriate function, given their lack of training in pediatrics, obstetrics and gynecology and the surgical subspecialties such as orthopedics and proctology, continues to be a highly debatable issue. A recent survey by Reitemeier et al.[4] indicates that, of 768 internists trained at Mayo Clinic and now practicing elsewhere, 82% believe that internists should provide primary care in the cities, but 89% of the internists believe that family physicians should provide primary care in rural areas; it is interesting that three-fourths of this same group believe that a better geographic distribution of physicians would improve the delivery of health care in this country.

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Address reprint requests to Dr. Thompson.

The term "ambulatory care" is mentioned as competing with primary care[3] also, which the AAFP has recently defined.[5] "Primary care is a type of medical care delivery which emphasizes first contact care and assumes ongoing responsibility for the patient in both health maintenance and therapy of illness. It is personal care involving a unique interaction and communication between the patient and the physician. It is comprehensive in scope and includes the overall coordination of the care of the patient's health problems, be they biological, behavioral, or social. The appropriate use of consultants and community resources is an important part of effective primary care."

In Great Britain, primary and ambulatory care are synonymous because the primary physician's role ends at the hospital door. Indicating the ubiquity, if not prevalence, of that concept, Petersdorf[6] said at a recent meeting of the Institute on Primary Care (sponsored by the American Association of Medical Colleges), "We really should give serious consideration to defining the family physician as an expert in ambulatory medicine and to having him turn his patients over to a hospital-based specialist when hospitalization is required." Even if one accepts this characterization of the family practitioner's role (and few family physicians do), it has been suggested that the training of such a specialist in ambulatory medicine would closely approximate the family practice residencies as they are designed today.

A Diagrammatic Definition

One should attempt, then, to identify as distinct entities the roles of the family practitioner, the primary physician, and the ambulatory-care physician. Diagrammatically, this distinction may be represented as shown in Figure 1. All family practitioners are engaged in primary care. Although primary care specialists generally, and family practitioners in particular, may practice only ambulatory medicine, most do not limit themselves to the outpatient domain. Finally, some primary physicians may practice in the ambulatory setting (shaded area) and not be family practitioners because they do not treat all age groups, do not assume longitudinal responsibility for the patient's health, do not treat the patient in health as well as in disease states, and do not deal with the patient in his family setting in a specific and deliberate way.

The relationships diagrammed in Figure 1 are self-evident. Now let us turn to a conceptual profile of a "typical" family practitioner, which serves as a flexible model that can be altered to fit several circumstances: (1) to fit the needs and personality of the individual physician, enabling him to "do what I like"; (2) to interrelate the family practitioner with his professional microenvironment, so that he can "do what no one else is doing"; and (3) to allow the family practitioner to adapt his skills to the demands of his patient community, in order to "do what I have to." Figure 2 represents a profile of a hypothetical family practitioner's time commitment.

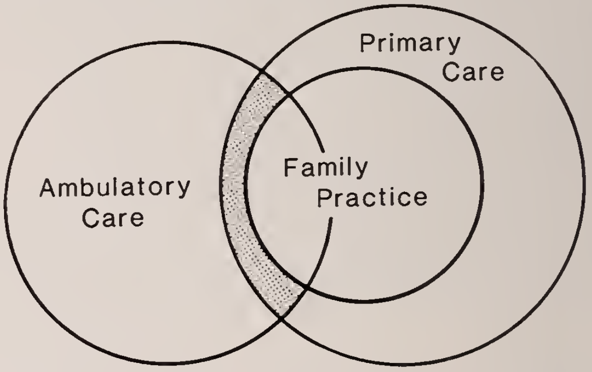

Fig. 1—Overlapping of family practice and primary care in ambulatory care medicine, indicating an area of ambulatory primary care that is outside family practice. Diagram does not indicate proportionality.

This practitioner spends 20% of his time in the hospital, taking care of routine obstetric cases, internal medicine problems (including coronary care unit with consultation), and one or two surgical procedures each week from his repertoire of five operations (vasectomy, dilatation and curettage, appendectomy, tonsillectomy, and hemorrhoidectomy). Because there are two pediatricians in his area, he has chosen not to care for hospitalized pediatric patients. He does, however, care for children as outpatients. He does obstetrics—even though there is one practicing obstetrician on his hospital staff—because he considers it a cornerstone of family practice (his own belief) and he enjoys it.

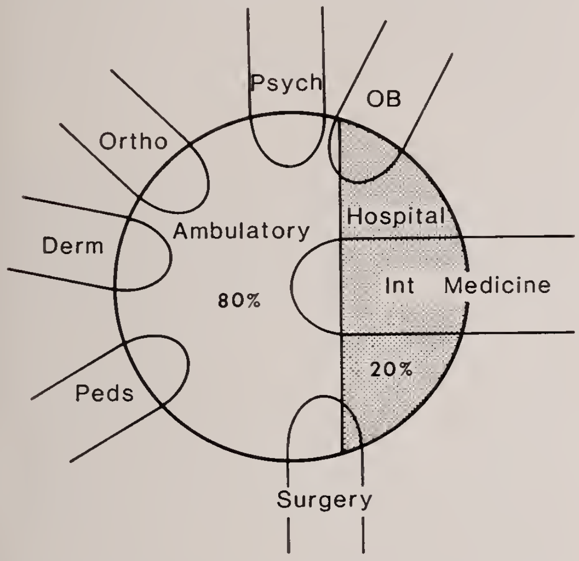

Fig. 2—A hypothetical family physician's practice profile. Diagram does not indicate proportionality except in the division between ambulatory and inpatient practice.

We note also that he is not cowed by psychiatric problems, although he confines his activity to outpatient care in one or two areas: marital counseling, which he enjoys and for which he has received specific postgraduate training and has attended weekend seminars, and the care of alcoholic patients. He does not enjoy looking after alcoholics but recognizes a need within his community for this service. He has spent three days at an alcoholic treatment unit, has read the AMA's manual on alcoholism, reads journal articles on alcoholism, and is familiar with local chapters of Alcoholics Anonymous and other resource services at the community, county, and state levels. Also, because of the time spent as an observer at the alcoholic treatment unit, he knows the director and counselor and can refer patients comfortably and get consultations.

According to this flexible model, then, we have a community-based physician who has electively and purposefully modified his postgraduate training to do what he likes (e.g., obstetrics, marital counseling), what he has to do (tonsillectomies, outpatient pediatrics), and what no one else is doing (seeing that alcoholics are referred to special resources). With this model, the possibilities for variation are limitless, as is the case in actual practice. Any family physician can design his own profile.

In caring for all age groups, and cutting across all disciplines, our model family practitioner uses medical consultants, paramedical counselors, nurses, social workers, clergymen, public health nurses, audiologists, the division of vocational rehabilitation, and others. In this way he does not feel so much as if he is fighting a holding action; he can deal more intensively with many problems, which can be followed up and reevaluated by the appropriate specialists and allied health professionals rather than by the physician himself.

Obviously, the mode of practice described is not a narrowly "medical" one, confined to direct intervention to help sick or injured patients. Today's family physician has left that kind of practice far behind. Now, family practice represents a broad interaction with society in many forms. Johnson[7] recently delineated some of these factors in an article striving to clarify objectives for family practice. As he noted, family practice must extend far beyond a concern with pathology and therapy, coordinating epidemiology, anthropology, and sociology with the more traditional disciplines.

It may be argued that the model we have chosen is arbitrary and does not represent what the "average" family practitioner is doing. We suggest that it is easier to define what the "average" specialist or subspecialist is doing and it is more difficult but no less germane to determine norms for family practitioners if they are doing their work in response to community requirements.

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Classified Advertisements

(Continued from page 246)

GENERAL PRACTITIONER to join MD in new Clinic in community of 2200; 25 miles southwest of Minneapolis; excellent schools and churches; productive farming area; 10-minute drive to hospital. Write or call Paul A. Stahler, M.D., Amo Vitae Clinic, 310 Sunset Drive, Jordan, Mn. 55352 612-492-6323.

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FAMILY PRACTICE PHYSICIAN or internist wanted to join three family practitioners and one surgeon. Mpls. suburb. Crystal Medical Clinic, 5636 W. Broadway, Minneapolis, Minn. 55428. Phone: (612) 537-8413.

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Malabsorption

RALPH A. FRANCIOSI, M.D.*

MALABSORPTION IS the inability to absorb "food" from the small intestine. Theoretically a variety of defects could cause malabsorption e.g. increased small bowel motility, mucosal alterations, intestinal enzyme deficiencies, pancreatic enzyme deficiencies and obstructive biliary disease. In a practical sense, one can consider malabsorption in infants and children as due to one of the following: increased small bowel motility, mucosal alterations and pancreatic enzyme deficiency. Increased small bowel motility is usually associated with Giardia infection or regional enteritis. Alterations in the small bowel mucosa are usually related to celiac disease (intestine sensitivity to wheat, rye and oats). Cystic fibrosis of the pancreas decreases pancreatic enzyme secretion into the small intestine and therefore is associated with malabsorption.

The approach to a patient with malabsorption begins with a thorough history and physical examination. The relationship between introduction of various foods and onset of malabsorption is important. The physical examination should record the height and weight as well as noting the abdominal girth and any wasting of subcutaneous fat and muscle. Rarely one might observe clubbing of the fingers and toes which would indicate severe lung disease, such as that in cystic fibrosis or severe liver disease.

The laboratory approach to malabsorption has been unnecessarily cumbersome and costly. In a practical sense, 95% of malabsorption cases can be handled in the following manner. The gross appearance, pH and reducing substances in the stool are measured. In malabsorption, the stools are bulky and foul smelling. The normal stool pH is seven and in malabsorption is six or lower. The acidity of the stool is related to the excess excretion of sugars from dietary sources. This excess number of sugars decreases the pH (increases acidity of the stool) and gives a positive test for reducing substances.

A stool smear which is air dried and stained with Wright's stain will reveal the presence of leukocytes which can be seen in inflammatory bowel disease. A stool culture should be performed to rule out pathogens associated with diarrhea. A preparation for ova and parasites will detect Giardia.

A D-xylose absorption test is helpful in differentiating malabsorption due to intestinal wall defects versus pancreatic enzyme defects. D-xylose is a five carbon sugar that is absorbed through the small intestine. This sugar does not require prior hydrolysis before absorption and therefore is a measure of the ability of small bowel to absorb. The D-xylose is given in a specific dose and blood samples are collected at 30, 60 and 120 minutes. A blood level of D-xylose 20 mg/dl or greater indicates normal absorption. The 120 minute sample is collected since a few patients show delayed gastric emptying and hence, could falsely be interpreted as low absorbers. We have found it extremely helpful that infants (less than two years) have a tube inserted into the duodenum from which pancreatic secretions can be collected and then the measured dose of D-xylose given. This approach has alleviated the problem of vomiting of an oral dose and confusion as to the amount of dose given.

If the D-xylose is normally absorbed, the pancreatic enzymes must be evaluated since the bowel wall is intact. A crude measure of the presence of pancreatic enzymes is the digestion of x-ray film by stool. One must remember that the trypsin present in stool which allows digestion of gelatin may be present due to bacterial action and may not properly indicate that the trypsin originated from the pancreas.

An abnormal D-xylose test requires a small bowel biopsy, which in the proper hands is a safe procedure. Knowing the clinical problem and extent of work-up, the biopsy then can be viewed histologically and possibly enzymatically.

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*Children's Health Center, Minneapolis, Minnesota.

Summary

The approach to the problem of malabsorption in children need not be cumbersome and costly. An organized approach should document 95% of cases presenting as malabsorption. The approach as outlined herein is utilized at the Children's Health Center and is both practical and rewarding.

Cover Photograph

"Mrs. Bunyan's Son, Paul"

Dr. William T. Luckey's son, Robert, labeled the cover photograph when he first saw the slide. The photo was taken in August of '72 at the Paul Bunyan Center in Brainerd, Minnesota.

Dr. Luckey is a psychiatrist practicing in Minneapolis, and has been active in amateur photography for over twenty years. He told the editors he became more involved in audiovisual slide programming the last few years, as photography may play a role in his clinical practice in the future. He does a fair amount of hypnotherapy and has been experimenting with the possibility of combining trance induction and audiovisual techniques. It now appears possible, he states, to conduct hypnotic sessions by pre-programmed audiovisual instruction.

As a photographer, his pet subjects are sports (especially the Vikings) and Minnesota landmarks. His camera is a Konica Auto-reflex-T with a zoom lens.

American Board of Family Practice

The American Board of Family Practice announces the next certification examination will be given October 30-31, 1976. The two day written examination will be held in seven cities geographically distributed throughout the United States. Information regarding the examination may be obtained by writing:

Nicholas J. Pisacano, M.D., Executive Director & Secretary
AMERICAN BOARD OF FAMILY PRACTICE, INC.
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Please note: It is necessary for each physician desiring to take the examination to file a completed application with the Board office. Deadline for receipt of applications in this office is June 15, 1976.

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Grand Rounds

Asymmetric Septal Hypertrophy

IRL J. DON, M.D.*

Asymmetric septal hypertrophy may appropriately be considered a cardiomyopathy. It presents in several forms, each of which may be a different stage of a single progressive disease. Free wall hypertrophy in patients with obstructive ASH may be a secondary phenomenon due to increased intraventricular pressure. When symmetric hypertrophy develops, subaortic obstruction may be reduced leaving a picture of non-obstructive cardiomyopathy. Continued long-term follow-up of large numbers of patients will be necessary to further elucidate the natural course of the disease and evaluate the modes of therapy.

ASYMMETRIC SEPTAL HYPERTROPHY (ASH) was first recognized in the late 1950's when symptoms typical of aortic stenosis, angina, syncope, and dyspnea on exertion were found in patients with a murmur of aortic stenosis but with a rapid upstroke of the carotid pulse. These patients at cardiac catheterization were shown to have an obstruction to left ventricular outflow. Left ventricular angiography demonstrated that during mid-systole the anterior leaflet of the mitral valve moved against an hypertrophied interventricular septum; this was thought to be the cause of the obstruction. The occurrence during mid-systole accounts for the initial rapid carotid upstroke. This entity was initially called idiopathic hypertrophic subaortic stenosis. Since that time it has become apparent that hypertrophy of the interventricular septum also occurs in the absence of outflow obstruction and that some patients without obstruction are symptomatic. ASH is now used to described a spectrum of conditions.[1]

Clinical Manifestations and Course

Adelman et al. analyzed the clinical course of 60 patients with hemodynamically proven ASH.[2] In 60% of the patients the murmur was the first sign of the disease. Ninety-three percent developed symptoms an average of 10 years after the murmur was first heard. Sixty-six percent deteriorated to functional class III-IV an average of five years after the onset of symptoms despite ventriculotomy and/or propranolol. These observations indicate that ASH is a progressive disease once the symptoms appear. However, there is extreme variability of the course of the diease among individual patients.[2]

Dyspnea, angina pectoris, lightheadedness, and syncope are the most common symptoms. In patients with moderate obstruction to left ventricular outflow, examination of the chest reveals a prominent apical impulse lateral to the mid-clavicular line and a left ventricular heave. A systolic thrill may be palpable over the lower precordium. The peripheral pulses are normal and a prolonged carotid upstroke is not present. A loud, harsh systolic murmur is heard over the entire precordium, but is most prominent at the apex and along the lower left sternal border. The murmur may radiate to the axilla. In most patients, the murmur is not heard well in the second right intercostal space or over the carotids. Paradoxical splitting of the second heart sound may be present.[3]

Etiology

Various causes for ASH such as environmental, infectious agents, and hypertension have been suggested; but none have been proven. A recent study by Clark et al.[4] demonstrates a high prevalence of ASH in families of patients with obstructive and nonobstructive ASH. Parents and children of 21 patients with obstruction and nine without obstruction were studied with echocardiography. Of the 30 index patients, 28 had at least one relative with ASH. Forty-six percent of all of

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the 105 relatives studied had ASH. An equal number of males and females were affected; affected males often had affected fathers. Therefore, the transmission of ASH is not X or Y linked. One affected member was found in 75% of the families in which two relatives were examined; this is consistent with an autosomal dominant mode of transmission. In only one family were both parents normal.

It was concluded that ASH is a genetic defect transmitted as an autosomal dominant trait with a high degree of penetrance.[4,5]

Pathology

The anatomic hallmark of ASH is hypertrophy of the interventricular septum disproportionate to that of the free wall of the left ventricle. In an autopsy study of 40 patients with ASH, Roberts found the ratio of the thickness of the septum to that of the free wall was greater than 1.3.[1] In hearts hypertrophied from other causes the ratio averaged 0.98 and in normal hearts 0.95. The endocardium of the left ventricular outflow tract which comes into contact with the anterior leaflet of the mitral valve is thickened by fibrous tissue. The anterior leaflet itself is also thickened. The thickening is presumably a direct result of the repeated contact of the two structures during systole. The occurrence of this thickening in patients who did not have obstruction at cardiac catheterization might be due to the rapid opening of the anterior mitral leaflet during diastole and contact with the septum at that time. This mechanism might also contribute to the thickening found in the obstructive form of ASH.

The characteristic histologic abnormality of the ventricular septum is the presence of areas of disarray of myocardial cells. These are interspersed among areas of muscle cells that are hypertrophied but normally arranged. Within some of these myocardial cells, myofibrils and myofilaments have also been found to be coursing in different directions rather than in parallel. Disorganized cells are rarely found in the ventricular free walls of patients with obstruction, but are widespread in the ventricular walls of symptomatic patients without obstruction.

Complications and Associated Conditions

In two large series including 246 patients with ASH, there were 12 patients with infective endocarditis. Endocarditis has been localized at the mitral valve, the aortic valve and the endocardial surface of the hypertrophied septal region.[6]

Oran et al.[7] during a two-year period diagnosed eight patients with concomitant ASH and coronary artery disease by cardiac catheterization and coronary angiography. Only two of the patients had significant ventricular outflow obstruction at rest. All of the patients were diagnosed clinically as having only coronary artery disease. The presence of both of these disorders in these eight patients represents a greater than chance association, but there is no evidence that coronary atherosclerosis is an etiological factor in ASH. Since ASH and coronary artery disease may mimic each other, it may be clinically very difficult to detect their coexistence. It is important to recognize these two diseases because drugs used to treat coronary artery disease, such as digitalis and vasodilators, increase left ventricular outflow obstruction.[7,8]

Kossowsky[9] reported a 61-year-old man with an anteroseptal myocardial infarction and ASH. Coronary angiography when a significant outflow obstruction was measured was normal. Six months later the patient was admitted to the hospital with an unequivocal acute transmural infarction. After recovery, angiography showed obstruction of the left anterior descending coronary artery and loss of the outflow tract obstruction presumably because of the site of the infarction.

The occurrence of ventricular asystole causing syncope after exercise has been described in a patient with obstructive ASH.[10] Syncope after exercise is common in patients with ASH because this is the time when obstruction to left ventricular outflow is the greatest. However, ventricular arrhythmias may be fatal with or without obstruction to left ventricular outflow. Demonstration of these arrhythmias in any patient is important because sudden death may be prevented by prophylactic insertion of a pacemaker.[10]

There has been a report[11] of a patient with obstructive ASH admitted to a hospital three times in cardiogenic shock. No diagnosis of myocardial infarction could be made, but ASH was diagnosed by echocardiography and cardiac catheterization. The shock was probably due to moderate fluid depletion, which would result in decreased ventricular systolic volume and increased sympathetic nervous activity and, in turn, lead to increased outflow obstruction. Cardiogenic shock may be one of the causes of sudden death in patients with ASH. Treatment with drugs that increase myocardial contractility would probably be fatal in shock associated with obstructive ASH.

Atrial fibrillation, abnormalities in atrioventricular conduction, pulmonary hypertension and obstruction to right ventricular outflow have been observed in a significant number of patients with ASH.[12,13] There have also been several reports of ASH associated with Friedreich's ataxia.[14]

Diagnosis

Various maneuvers can alter the degree of obstruction and, hence, the intensity of the murmur. These can be of help in differentiating the murmur of ASH from other systolic murmurs. Anything that increases arterial pressure, decreases myocardial contractility or increases left ventricular volume will decrease the degree of obstruction and the intensity of the murmur. Anything that will produce the opposite effects will lead to an increase in the obstruction and intensity of the murmur.[1,15]

Several investigations have shown echocardiography to be a highly sensitive, noninvasive technique for the diagnosis of ASH. Tajik and Giuliani[16] have made several echocardiographic observations in patients with ASH. The septal abnormalities consist of increased width, asymmetric hypertrophy, and decreased contraction and amplitude of excursion. There are also three abnormalities of mitral valve motion: systolic anterior motion, diastolic apposition against the ventricular septum and decreased diastolic closure rate. An abnormal midsystolic closure followed by a late systolic opening of the aortic valve has been noted in patients with ASH.

Simultaneous echocardiography and cardiac catheterization have shown abnormal systolic anterior motion of the mitral valve when no left ventricular outflow tract gradient was recorded. Obstruction is not simply a result of movement of the mitral valve against the septum, but is probably also a function of the duration and area of contact. While echocardiography may be useful for detecting the various anatomic abnormalities in ASH, it does not necessarily reveal the degree of obstruction. However, if, in a given patient, there is an initial baseline correlation of echocardiography with hemodynamic studies, then echocardiography may be useful for serial indications of the change in degree of obstruction.[17]

Other investigators[18] have found the presence of antiheart antibody in nine of 11 patients with ASH. They also found decreases in levels of antiheart antibody with clinical improvement of the disease. Antiheart antibody is present in other cardiac diseases. Therefore, while its presence may be consistent with ASH, it is certainly not pathognomonic.

Treatment

In symptomatic patients with significant outflow obstruction, surgery was the treatment of choice until the mid 1960's when propranolol became available. Since that time the number of patients undergoing operation has decreased. Currently, Tajik and associates[19] recommend surgery only for those patients who do not respond to propranolol. Adelman[2] advocates surgery in asymptomatic patients only when they have severe, persistent resting obstruction and a family history of sudden death, or when their activity can not be limited.

Various surgical techniques have been devised, but good long-term results have been consistently obtained only with division or resection of the hypertrophic muscle of the left ventricular outflow tract. Tajik[19] reports a study of 43 patients, 36 of whom underwent myectomy and one myotomy. The other six patients underwent a surgical procedure in addition to myectomy or a procedure that is no longer recommended. Four of these six patients died during surgery while only three of the 37 patients undergoing simple myectomy died during surgery. One patient was lost to follow-up, and there were four late, sudden deaths occurring more than six months after surgery. The remaining patients were followed for a mean of 84 months. Before surgery, three patients were in functional class I, nine were in class II and 31 were in classes III and IV. At completion of the study 14 were in class I, 14 were in class II, and three were in classes III and IV.

Epstein et al.[20] studied 68 patients who underwent myectomy or myotomy. All were in functional classes III or IV prior to surgery. Of 55 patients followed for one year or more after surgery, 24 were asymptomatic and 31 were in functional class II. Operative mortality was 9%.

In an investigation by Adelman,[2] 75% of patients in classes III and IV who underwent myotomy had sustained symptomatic improvement into the second postoperative year, while only 25% of classes III and IV patients receiving propranolol maintained improvement for the same period of time.

Cooley and co-workers[21] have recommended excision and prosthetic replacement of the mitral valve as the operation of choice. Other investigators feel that this is not an appropriate procedure because the valve itself is intrinsically normal. Echocardiograms in patients who have had ventricular septal myectomies demonstrate a more normal mitral valve motion along with an increase in outflow tract dimension. Mitral regurgitation is often found in patients with ASH and is also corrected by myectomy.[21,24]

Two independent studies[25,26] have been performed to determine the prognosis following orally administered propranolol and to correlate this with the response to propranolol administered intravenously at the time of cardiac catheterization. The daily oral propranolol doses ranged from 40 to 240 mg. In most patients, symptoms diminished or stabilized during therapy with oral propranolol. There was greater improvement in dyspnea than in angina or syncope. The initial clinical response correlated with the reduction of outflow obstruction that occurred after IV propranolol. The long-term clinical course correlated with the hemodynamic findings at the follow-up catheterization. The severity or lability of the outflow obstruction during the initial catheterization did not have predictive value for the response to long-term oral propranolol therapy.

In one of the studies,[26] after the initial favorable response to propranolol, approximately the same percentage of patients showed a clinically stable, improved, or deteriorated condition as was observed in a series of untreated patients.[12] This finding indicates that propranolol does not affect the progress of the underlying disease process or the clinical course.

Symptomatic patients with the non-obstructive form of ASH present a therapeutic dilemma. Propranolol seems to be effective in relieving chest pain. However, the benefit of propranolol is questionable for patients who are mainly limited by dyspnea or fatigue. Because there is no obstruction to ventricular outflow, and because the histologic lesions are found throughout the septum and the ventricular free wall, surgery plays no part in the treatment of nonobstructive ASH.[1]

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In Memoriam

Fred P. Moersch, M.D.

Dr. Frederick P. Moersch, 86, a retired Mayo Clinic neurologist, died December 28, of a heart attack at his Ft. Lauderdale home. He had moved to Florida in 1956 when he retired after 36 years on the Clinic staff.

Born in St. Paul, Dr. Moersch earned his medical degree at the University of Minnesota Medical School. He was noted for his work in neuropsychiatric ailments. He was a former president of the American Board of Psychiatry and Neurology and a member of a score of state, national and international organizations.

His wife, Agnes; a son, Dr. Robert Moersch, Ft. Lauderdale surgeon; and a daughter, Virginia, survive him.

Alton C. Olson, M.D.

Dr. Alton C. Olson, medical doctor at Tyrol Clinic in Golden Valley, died November 30. He was 67.

His medical education was obtained at the University of Minnesota Medical School, and in addition to being a member of the American Medical Association, Dr. Olson was a member of the Hennepin County Medical Society and the Minnesota State Medical Association.

His wife, Elizabeth; two sons, Curtis and George; and two daughters, Ginger and Mary, survive him.

Raymond J. Dittrich, M.D.

Dr. Raymond Dittrich, 78, St. Paul orthopedist, died January 1. He was born in New Ulm, Minnesota, and obtained his education at the University of Minnesota Medical School.

He was a member of the American Medical Association, a Diplomate of the American Board of Orthopaedic Surgery, and a Fellow of the American Academy of Orthopaedic Surgeons. In addition he was a member of the Ramsey County Medical Society and a Life and 50 Club Member of the Minnesota State Medical Association.

Dr. Dittrich is survived by his wife, Helen, and two sons, Dr. J. Paul Dittrich of Anchorage, and Raymond J.

Harlow J. Hanson, M.D.

Dr. Harlow J. Hanson, 83, Minneapolis surgeon, died January 11. He earned his medical degree at the University of Illinois Medical School.

Dr. Hanson began his practice in New London and in the winter his only means of travel was with horse and sleigh. In 1925 he moved to Minneapolis where in addition to his practice, he was health officer for the City of Bloomington for 34 years.

He was a member of the American Medical Association, the Hennepin County Medical Society, and a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Hanson is survived by his wife, Gladys.

Richard B. Ellingson, M.D.

Dr. Richard B. Ellingson, 47, Minneapolis ophthalmologist, died December 29. He was born and educated in Minneapolis and finished his post-graduate work at the Mayo Clinic.

Dr. Ellingson was a Clinical Instructor at the University of Minnesota Medical School and a member of the American Medical Association, the Minnesota State Medical Association, and the Hennepin County Medical Association.

He is survived by his wife, Helen, a daughter, Kirsten, and two sons, Stephen and David.

Carl W. Krause, M.D.

Dr. Carl W. Krause, 72, Fairmont physician, died October 6. He was born in Alpha, Minnesota, and earned his medical degree from the University of Minnesota Medical School. Before going to Fairmont, Dr. Krause practiced in Preston for over a year.

He was a member of the American Medical Association, the Blue Earth Valley Medical Society, and the Minnesota State Medical Association.

LaVern C. Strough, M.D.

Dr. LaVern Strough, 60, who died December 28, was born in Beatrice, Nebraska, and educated at the University of Nebraska Medical School. He completed his fellowship in Neurology and Psychiatry at the University of Minnesota Medical School. In 1968 he joined the Worthington Clinic in Worthington.

He belonged to numerous scientific and professional societies and had written a number of articles.

Dr. Strough is survived by his wife, Dorothy, and one daughter.

Elvin F. Englund, M.D.

Dr. Elvin F. Englund, 58, Minneapolis internist, died January 18. His education was obtained at the University of Minnesota Medical School, and he interned at the Swedish and Minneapolis General Hospitals.

He was a member of the American Medical Association, the Minnesota State Medical Association, and the Hennepin County Medical Society.

His wife, Glennis; daughter, Mrs. Meredith Howell; and sons, Dr. John F. Englund, Paul and Craig, survive him.

Harry E. Bank, M.D.

Dr. Harry E. Bank, 84, Minneapolis internist died September 1. A native of Milwaukee, Wisconsin, Dr. Bank attended the University of Minnesota Medical School. His post-graduate work was completed at Veterans Hospital in Palo Alto, California.

He was a member of the American Medical Association, the Hennepin County Medical Society, and an Associate Member of the Minnesota State Medical Association.

Dr. Bank is survived by his wife, Marian.

James E. O'Donnell, M.D.

Dr. James O'Donnell, 91, Minneapolis surgeon, died November 1, of complications of an automobile accident. A native of Minneapolis, his education was obtained at Hamline University Medical School.

Dr. O'Donnell was a member of the American College of Surgeons, American Medical Association, Minnesota State Medical Association, and the Hennepin County Medical Society.

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Index to Advertisers

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Allied Medical Audit Control, Inc. 284
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Classified Advertising 246
Dahlberg Hearing Aids 212
Dow Pharmaceuticals 247, 248, 249, 250
Flint Laboratories 260, 261, 262
Kjell Bergh's Borton Leasing, Inc. 242
Lilly, Eli, & Co. 222
Loma Linda Foods 272
Medcalf Orthopedic Appliance Co. 284
Medical Protective Company 242
Northwestern Bell 216
Pharmaceutical Mfrs. Assn. 268, 269
Roche Laboratories .... Cover 2, 211, 236, 237, 238, Covers 3-4
Roerig and Company 235
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U.S. Navy Recruiting District 214
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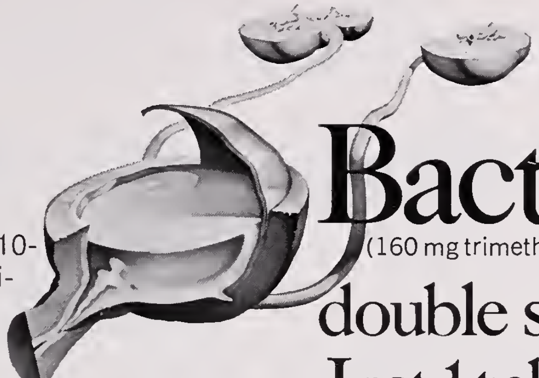

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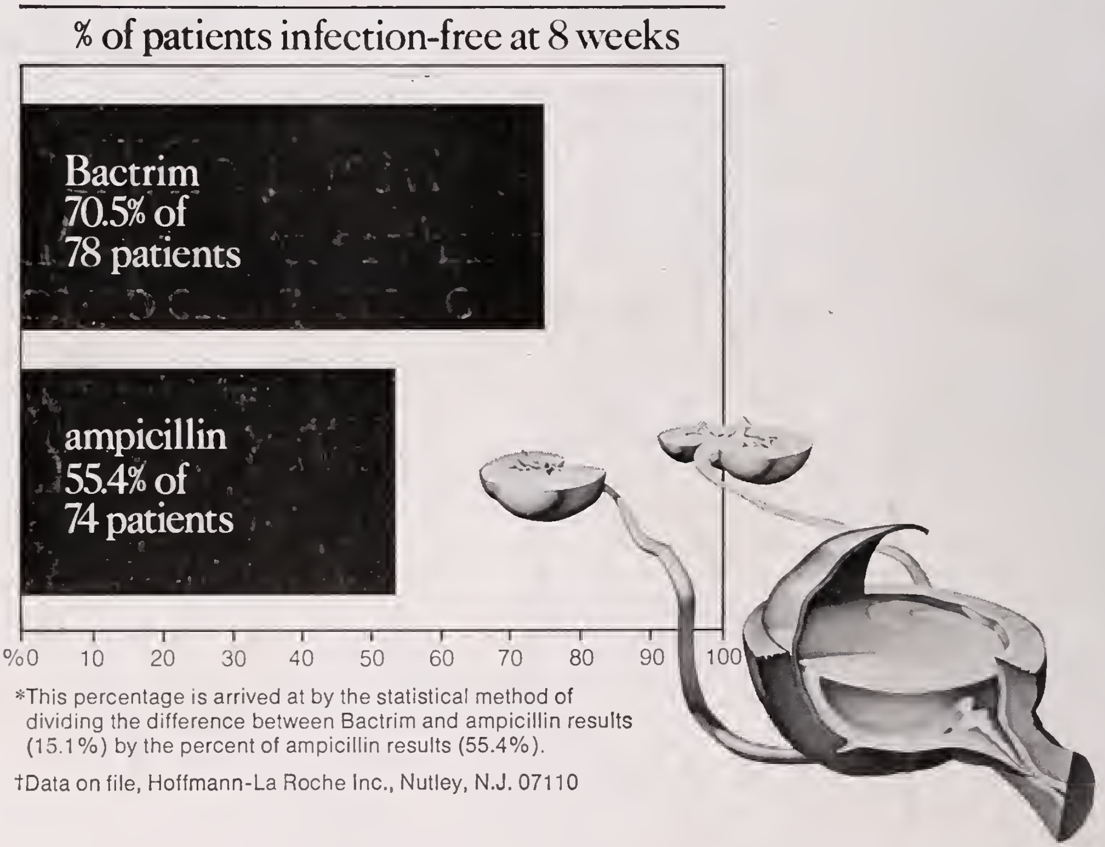

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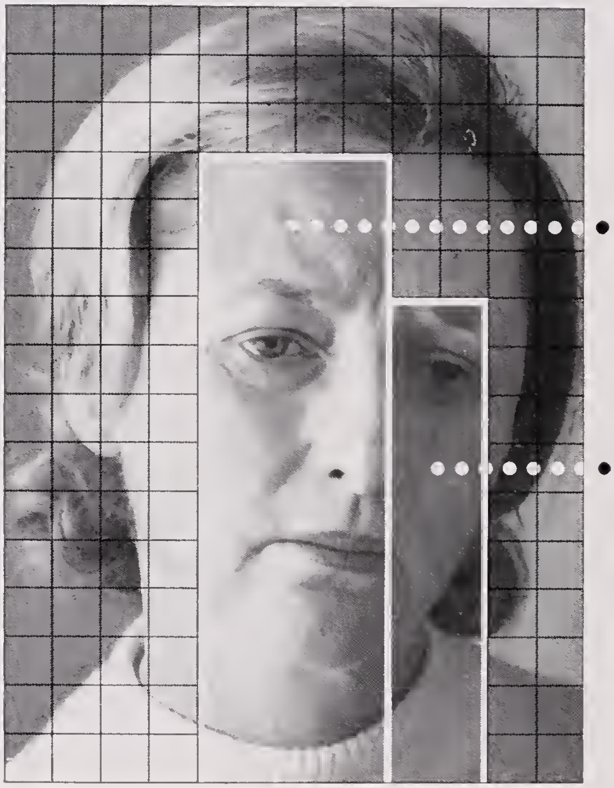
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President's Letter

Swan Song

When elected to this office almost a year ago, I looked ahead to the duties to be performed with varying degrees of concern, pleasure, and anticipation. I must confess that writing the President's Letter in MINNESOTA MEDICINE ranked near the bottom of the list of pleasurable obligations. However, with the encouragement of many and the kindly comments of some, as the months passed and the letters were published, I began to look forward to and enjoy the challenge of writing the next editorial. It has been a truly rewarding experience and enjoyable.

As I now critically review the President's Letters I have written, I am concerned that, in my attempt to discuss some of the issues and strongly urge physicians to be involved in the socio-economic and political arena as it affects our profession and our patients, I have inadvertently appeared to encourage physicians to adopt a defensive, scolding, complaining, frustrated, unhappy, and argumentative position and attitude.

In this last letter, my swan song, I want to clearly indicate what I believe the physician's position and attitude must be. Medicine needs an offensive posture, not defensive; medicine needs a strong position on issues supported by *all* physicians, not a position weakened by selfish interests and self serving factions; medicine needs optimism to free our frustrations, not pessimism to feed a defeatist attitude; medicine needs a willingness to discuss the issues and accept constructive changes in the system, not blind stubbornness against change; medicine needs continued insistence on high ethical standards for the protection of our patients, not commercialism and advertising to destroy professionalism; medicine needs the active and financial support of every physician, not the burden assumed by the concerned and dedicated majority alone.

I thank each of you for the honor and privilege you have given me to serve as your president. With this swan song, my letters are finished but, like you, my dedication and commitment to our profession continues.

G R Diessner

G. Roy Diessner M.D.
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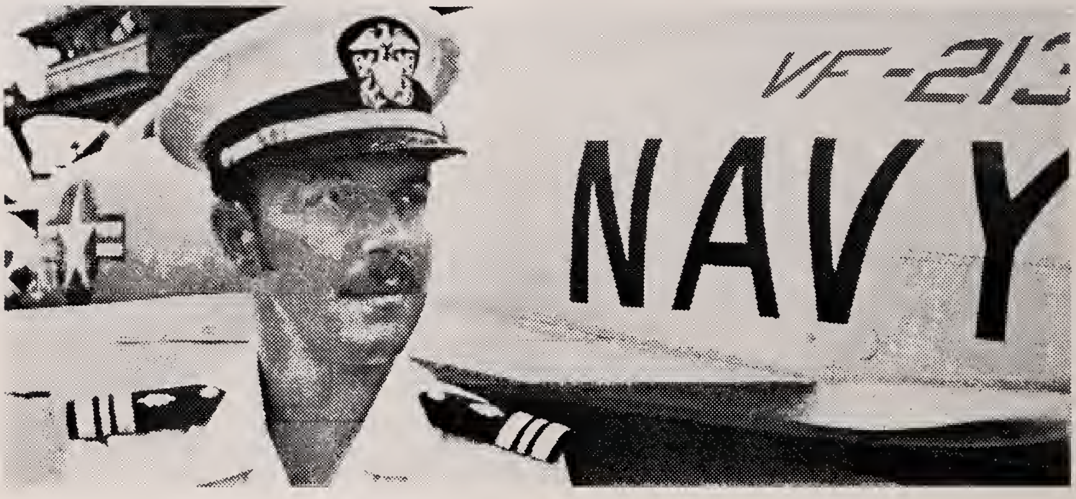

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Editor's Notebook

It Ain't Necessarily So

> *"Unnecessary surgery wastes lives and dollars. There were an estimated 2.4 million unnecessary surgeries performed in 1974 at the cost to the American public of almost $4 billion. These unnecessary surgeries led to 11,900 deaths."*
>
> Conclusion of Report, Subcommittee on Oversight and Investigations of the Committee on Interstate and Foreign Commerce (House of Representatives), Cost and Quality of Health Care: Unnecessary Surgery. Washington, DC, US Government Printing Office, January 1976.

> *"It is not the function of our government to keep the citizens from falling into error; it is the function of the citizen to keep the government from falling into error."*
>
> Justice Robert H. Jackson as quoted in *Reader's Digest,* August, 1958.

Since the Congressional Subcommittee released its report, the phrase "unnecessary surgery" has been out and on the loose.

Major newspapers across the land have featured it; the three television networks have trumpeted it; and the newsmagazines—*Newsweek, Time,* and *U.S. News & World Report*—have flashed it before readers. All have written or spoken gravely of the dangers of surgery to the American public, but none have bothered to investigate the substance of the Subcommittee's report.

I would like to analyze the report and a related series of articles in the *New York Times.*

"Unnecessary Surgery" and "Avoidable Deaths"

I became aware of the "unnecessary surgery" issue when I read about it on February 1 in the *Minneapolis Tribune* and the Sunday issue of the *New York Times.* The *Tribune* dutifully parroted the Subcommittee's conclusions, already quoted above. But the *Times* summarized its own series of articles on incompetent doctors, "unnecessary surgery," and "avoidable deaths."

New York Times' "Projections"

Here, for perspective, are the Times' "projections" for the practice of surgery in the United States in 1975.

Number of Operations	Surgery Not Recommended	Deaths	Avoidable Deaths
Tonsillectomy, 724,000	70%	150	105
Cholecystectomy, 472,000	14%	6700	938
Hysterectomy, 787,000	22%	1700	374
Prostatectomy, 223,000	29%	2700	783

In a footnote to the table listing this information, the *Times* said it based its estimate of avoidable deaths on: "The Cornell study and the New York Times' projections."

Basis for Death Estimates

When you carefully read the *Times* piece and the Subcommittee report, you learn two things: 1) both rely on the Cornell study as an authoritative source for calculating "unnecessary" operations; and 2) the *Times* and the subcommittee use different sources for surgical mortality figures. The *Times* got its information from the National Center of Health Statistics, a unit of HEW's Public Health Service. The death rate included all operations in the United States. The Subcommittee, on the other hand, garnered its information from the Commission on Professional and Hospital Activities (CPHA) of Ann Arbor, Michigan. The CPHA data also included all patients in United States operated upon and discharged dead. So far, so good.

Cornell Study, or McCarthy Report

What is the Cornell study?

In the December 19, 1974 issue of the *New England Journal of Medicine,* Doctor Eugene McCarthy, an M.D. with a Masters Degree in Public Health, and Geraldine Widmer, a nurse who also holds a Masters Degree in Public Health, published a controversial paper: "Effects of Screening by Consultants on Recommended Elective Surgical Procedures."

Rather than analyze McCarthy and Widmer's paper, I shall reprint the abstract of their paper:

> **Abstract** To assess the need for elective operations recommended to a group of union members, 1356 self-selected patients were re-examined by board-certified specialists. Approximately 24 percent of all procedures recommended were not confirmed. An additional 2.1 percent were confirmed but did not require hospitalization. The proportion of cases not confirmed in each of the surgical specialties were as follows, in descending order of frequency of utilization: general surgery, 16.4 percent; gynecology, 31.4 percent; orthopedics, 40.3 percent; ear, nose and throat, 16.3 percent; ophthalmology, 28.2 percent; and urology, 35.8 percent. Program operating costs were about one eighth of the estimated savings from hospitalizations not required. Because of the cost savings and the demonstrated percentage of operations not approved, presurgical screening programs appear to have a substantial benefit for any insured population. (N Engl J Med 291:1331-1335, 1974)

Had the *Times* and the Congressional Subcommittee members bothered to read the original article, or even the abstract, I'm sure they would not have fallen into the error of making unfounded extrapolations.

Errors of Extrapolation

In the first place, "1356 self-selected patients" belonging to unions in and around New York City, hardly constitutes a cross-section of American Medicine. Besides, the number of patients is small, too small, to generalize from.

Second, to judge categorically that an operation the personal physician recommends is "unnecessary" because a surgical consultant "did not confirm" the procedure strikes me as absurd. To declare from such reasoning that 17 percent of all operations performed in the United States are "unnecessary" compounds the absurdity. It ain't necessarily so. What were the credentials of the personal physicians who recommended surgery? What was the bias of the consultants? What were the criteria the consultants used to reject procedures? And, finally, who is to say the second opinion was any better than the first? Also I find no mention in the McCarthy paper of followup studies on patients who did not undergo surgery. Did any, for example, subsequently have attacks of cholecystitis? Anyway, McCarthy and Widmer admit in their paper: "As a result of a number of factors, the findings presented here cannot be applied to the general population undergoing elective procedures."

Third, as every seasoned clinician knows, most operations do not fall neatly into "necessary" or "unnecessary" categories. Take cholestectomy for gallstones, or subtotal gastrectomy for chronic gastric ulcers, or demand abortion in the first trimester of pregnancy, or Caesarian section for prolonged labor, or hysterectomy for minor bleeding, or prostatectomy for intermittant urinary tract obstruction? Who is to judge whether these procedures should be done? The patient's physician or an outside consultant? In the cases of elective cholestectomy, Ingelfinger says of the McCarthy report: ". . . one may assume that at least a third of the second opinions were in error, especially since many of the indications for elective removal of gallbladders are highly controversial."[2]

Fourth, both the *Times* and Congressional Subcommittee based their "unnecessary" rate on *elective* procedures, then erroneously applied this rate to all operations —elective, urgent, and emergency. For example, on page 33 of the Subcommittee report, this statement appears: "Dr. Virgil Slee, President of CPHA, estimated that of 7,600,000 patients operated upon during the first six months of 1975, 105,000 patients were discharged dead. That estimate represents a mortality rate of 1.4 percent."

But that estimate also implies the patients died from their surgery. Which isn't so. Many patients, no doubt, were desperately ill from trauma, or congenital defects, or widespread malignancy, or an infarcted or ruptured viscus, or gangrenous legs, or leaking aneurysms. They died, not of surgery, but the underlying disease. But the Subcommittee says its members knew 1.4 percent for all operations was too high, so they took a "conservative" figure of 0.5 percent. And where does the 0.5 percent figure come from? From a crude guess by an author who was comparing operations and surgeons in the United States, England, and Wales.[3]

Government Logic

Anyway, if you take the 0.5 percent guess, which is a conservative scaling down of the 1.4 percent figure, which in turn was based on "unpublished data," and multiply it by 2.38 million "unnecessary" procedures, which were not performed on 1356 New York union members because the procedures were "not confirmed" by a surgical consultant, you can conclude, as the Subcommittee did, that ". . . the number of deaths from unnecessary surgeries approximates 11,900 for last year."

A Surgeon's Comments

Doctor Francis Moore, Professor of Surgery at Harvard Medical School, had this to say about the *Times'* and Subcommittee's statistics: "These figures are wrong . . . anybody who knows anything about surgical statistics knows these numbers are impossible . . . They equate disagreement with surgical indications with lack of necessity . . . That's wrong. And they equate doing an operation on which there's disagreement with incompetence . . . My arithmetic will show the avoidable death rate at least one-tenth and perhaps one-fifteenth of the figures reported by the *Times*.[4]

Closing Remarks

Why did the Congressional Subcommittee and the *New York Times* distort and bloat the figures on surgical deaths? I suspect the reasons are not as sinister as many physicians might think. Doctor Francis Moore's theory[4]—that junior HEW officials, frustrated with rising surgical costs, plucked the McCarthy report out of the *New England Journal* and fed it to the Subcommittee—sounds plausible to me. Moore also thinks the *New York Times* simply fell for the Subcommittee report because the report contained the news the *Times* wanted to hear.

What disturbs me about all this is the Congress's and the Press's shoddy investigative techniques and their lack of a fair and open mind. Congress and the press pride themselves on their "investigative" spirit, yet this spirit applies mostly to what these two institutions dislike. Give either one a report they like to hear, and Congressmen and press members drop their investigative approach and take an adversary stanch. Before congressmen or reporters release news that inflames the public and degrades the medical profession, I suggest they read the original source material, check out the facts, and say how they played with the figures to arrive at their conclusions.

Richard L Reece MD

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Contents—May, 1976

OVER PHOTOGRAPH—"Mayo Building—Mayo Clinic"
Donald A. Scholz, M.D. ... 337

RESIDENT'S LETTER—Swan Song
G. Roy Diessner, M.D., President ... 289

DITOR'S NOTEBOOK—It Ain't Necessarily So
Richard L. Reece, M.D., Editor-in-Chief ... 291

RIGINAL CONTRIBUTIONS

Sedimentation Rate in Polymyalgia Rheumatica
William F. Nuessle, M.D. et al. ... 297

Anti-i Hemolytic Anemia in Infectious Mononucleosis
James A. Walker, M.D. and Paul B. Dickinson, M.D. ... 301

Human Myiasis by the Black Blow Fly
Leon J. Damsky, Ph.D. et al. ... 303

DITORIALS

Hepatitis B
Claus A. Pierach, M.D. ... 315

Disseminated Gonococcal Infection
Mark V. Dahl, M.D. ... 317

Anti-i Hemolytic Anemia in Infectious Mononucleosis
Gene Hartmann, M.D. ... 317

Polymyalgia Rheumatica
Gene G. Hunder, M.D. ... 319

ETTERS TO THE EDITOR

Atopic Dermatitis
W. E. Walsh, M.D. ... 321

Poison Control Center
A. S. Manoguerra, Pharm. D. ... 321

AUSES OF DEATH OF INSTITUTIONALIZED PHENYLKETONURIC ATIENTS—A NATIONAL SURVEY
Robert O. Fisch, M.D. et al. ... 306

INNESOTA STATE MEDICAL ASSOCIATION—Annual Meeting
R. D. Semsch, M.D., Chairman, Scientific Assembly ... 326

PECIAL ARTICLE—Long Term Anticoagulant Therapy ollowing Myocardial Infarction
Douglas H. Johnson, Medical Student ... 333

ISTORY—Twenty-Five Years of Amalgamation of Psychiatry ith Obstetrics—Gynecology at the University of Minnesota
Irving G. Bernstein, M.D. et al. ... 341

ORONARY CARE

Acute Phase of Myocardial Infarction
A. A. J. Adgey, M.B., M.R.C.P. et al. ... 347

ONTINUING MEDICAL EDUCATION ... 300, 309, 346, 356

LASSIFIED ADVERTISEMENTS ... 325

NDEX TO ADVERTISERS ... 356

Volume 59, 5
Pages 285-356

MINNESOTA
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REPRESENTS

- Association of Neurologists of Minnesota
- Duluth Surgical Society
- Hennepin County Psychiatric Society
- Minneapolis Academy of Medicine
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Sedimentation Rate in Polymyalgia Rheumatica

Report of 24 Cases

WILLIAM F. NUESSLE, M.D.*; HAROLD E. MILLER, M.D.*;
FRANKLIN C. NORMAN, M.D.* and DAVID A. VAGNEUR, M.D.*

Polymyalgia rheumatica is a symptom-complex associated with giant cell arteritis. Early diagnosis with Prednisone therapy may prevent ischemic complications, including blindness. An elevated sedimentation rate is a vital diagnostic tool and guide to therapy.

THE CLINICAL SYNDROME of polymyalgia rheumatica is considered a manifestation of the collagen disease characterized pathologically by giant cell arteritis.[1,2,3] Polymyalgia rheumatica produces girdle myalgia, malaise, fatigue, low-grade fever and marked elevation of the sedimentation rate. Less significant laboratory findings include slight anemia, leukocytosis, decreased serum albumin and increased alpha globulin.[2] The prodromal symptomatology of polymyalgia rheumatica may alert the physician to giant cell arteritis with its ravaging ischemic complications, especially of the ocular vessels.[3,4]

We recently observed two patients with polymyalgia rheumatica in whom the elevated sedimentation rate preceded myalgia. We have reviewed our own patients with polymyalgia rheumatica with special interest in the erythrocyte sedimentation rate.

Cases No. 3-9 of the twenty-four polymyalgia rheumatica patients who are summarized in Table 1 were previously reported.[3,5] There were 23 women and one man ranging in age from 54 to 89 years. Corticosteroid therapy produced prompt

TABLE 1
Clinical Features of Twenty Four Patients with Polymyalgia Rheumatica

	Sex	Date of First Symptoms	Age at Onset	Myalgia	Gm Hgb	ESR	Biopsy	Complications
1	F	Nov 55	81	Back, Shoulders	10.2	53*	None	Blindness 1966; Died 1974
2	F	Sep 59	58	Neck, Head	12.0	100	None	Claudication
		May 74	73	Thighs	13.1	63	None	Recurrence; Claudication
3	F	May 60	72	Neck, Back, Thighs	10.3	108	None	Died 1975
4	F	Dec 63	75	Neck, Shoulders	12.3	78	Positive	Blindness; Died 1971 (Autopsy)
5	F	Apr 65	54	Back, Chest	11.9	108	Negative	Persistent disease
6	F	Jul 65	73	Arms, Thighs	12.7	88	Negative	In Tenth Year of Treatment
7	F	Nov 65	74	Back, Jaw, Thighs	12.0	78	Negative	Optic Neuritis
8	F	Jul 66	74	Neck, Jaw, Shoulders	12.9	109	None	———
9	F	Jun 66	82	Neck, Back, Thighs	11.5	80	Positive	Blindness
10	F	May 67	73	Head, Shoulders	12.2	91	None	———
11	F	Mar 67	60	Shoulders, Back, Legs	11.5	57	Positive	———
12	F	Sep 68	68	Neck, Back, Jaw	12.7	89	Positive	———
13	F	Mar 70	83	Thighs, Arms	10.6	58	None	Died 1973 (Autopsy)
14	F	Jun 71	66	Thighs, Head	15.8	95	Positive	———
15	F	Jul 71	70	Back, Shoulders, Head	12.2	71	Positive	———
16	F	Jan 72	81	Neck, Shoulders	12.4	90	None	Died 1974 (Autopsy)
17	F	Feb 73	77	Shoulders, Thighs	12.3	98	None	———
18	F	Oct 73	73	Back, Limbs	10.9	104	None	———
19	F	Nov 73	64	Shoulders, Thighs	13.4	100	None	———
20	F	Sep 74	89	Hips, Shoulders	10.7	94	None	Stroke
21	F	Dec 74	71	Back, Head, Jaw	12.6	98	None	———
22	M	Dec 74	68	Shoulders, Legs	11.8	82	None	———
23	F	Jan 75	69	Interscapular	13.1	71	None	———
24	F	Dec 74	71	Neck, Legs	10.5	112	None	———

*Wintrobe; Others Westergren

---

*Minneapolis, Minnesota.
See editorial, page 319.

relief of the myalgia and improvement in the sedimentation rate. Six of nine temporal artery biopsies showed giant cell arteritis. Unilateral blindness occurred in three individuals. Five died of coronary and cerebral arteriosclerosis two to 19 years after the polymyalgia, but autopsy showed no active arteritis in three. Prednisone in doses as low as 2½ mg. daily was used to control myalgia and sedimentation rate elevation for periods up to 10 years.

Case Reports

Case 1

An 81-year-old woman was seen on November 15, 1955 with pain in shoulder, back and thigh. She was brought to the Medical Arts office in a wheelchair, but no physical or laboratory abnormalities were found other than a sedimentation rate of 53 mm. (Wintrobe). Administration of 20 mg. of Prednisolone daily was followed by marked symptomatic improvement so that on revisit in two weeks, she could move with ease. The steroid was continued in doses of five to 15 mg. daily until August of 1958. Sudden blindness of the right eye occurred in 1966. She died of cerebral artery disease in 1974.

Comment

Polymyalgia rheumatica was diagnosed retrospectively. Steroids improved myalgia so that she left her wheelchair and was freely ambulatory in a two-week period. Unilateral blindness occurred 11 years after rheumatic symptoms, possibly from arteritis.

Case 2

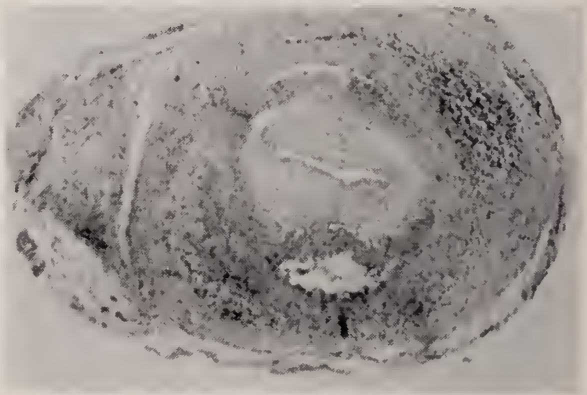
A 58-year-old woman was first seen on September 30, 1959 with severe myalgia of the neck and shoulders and intermittent claudication. There were no unusual findings other than an erythrocyte sedimentation rate of 100 mm. She was given brief courses of Dexamethasone and Triamcinolone, both of which relieved the myalgia with sedimentation rate improvement from 92 to 69 mm. Without therapy the sedimentation rate varied from 93 to 120 mm. during the next few months. On June 5, 1974 she was seen with thigh pain and claudication. The erythrocyte sedimentation rate was 63 mm, and a diagnosis of recurrent polymyalgia rheumatica was made. With 20 mg. of Prednisone daily, the pain disappeared and the sedimentation rate dropped to 26 mm. The myalgia remained well controlled on Prednisone therapy. When the patient stopped steroids on fearing side effects, the sedimentation rate increased to 97 mm. but again was controlled with Prednisone therapy (Table 2).

Comment

Although myalgic and arteritic symptoms may be protracted, this was the only case of recurrent polymyalgia rheumatica with a long symptom-free interval.

Case 11

This 61-year-old seamstress was first seen on September 27, 1967 with muscular pain of the shoulders, back and legs. In March of 1967 she saw another physician who found her sedimentation rate to be 91 mm. and provided relief with a brief course of steroid therapy. Examination elicited slight tenderness of the right temporal artery. The sedimentation rate was 57 mm. A biopsy of the artery on October 2, 1967 showed giant cell arteritis (Figure). Twenty mg. of Prednisone gave symptomatic relief in 24 hours. The patient has been maintained since then on 5 to 20 mg. of Prednisone daily.



Figure—A section of the temporal artery showing narrowed lumen, intimal thickening and granulomatous reaction with giant cells.

TABLE 2
The Erythrocyte Sedimentation Rate (Millimeters Per Hour) and Steroid Therapy in Recurrent Polymyalgia Rheumatica

Date	ESR	Daily Prednisone Dosage
27 Jan 56	46	
30 Sep 59	100	
02 Oct 59		2.25 mg*
08 Oct 59	92	
12 Oct 59		4 mg†
09 Nov 59	69	
20 Nov 59	93	
09 Dec 59	94	
22 Dec 59	97	
05 Jan 60	95	
25 Jan 60	102	
03 Mar 60	120	
21 Jun 60	109	
11 Apr 61	23	
05 Jun 74	63	20 mg
09 Jul 74	26	15 mg
13 Aug 74	48	20 mg
16 Sep 74	53	20 mg
29 Oct 74	97	30 mg‡
05 Nov 74	60	30 mg
26 Nov 74	11	20 mg
16 Dec 74	17	15 mg
07 Jan 75	20	12.5 mg
03 Feb 75	18	10 mg
24 Feb 75	32	12.5 mg
17 Mar 75	26	12.5 mg

---

*Dexamethasone
†Triamcinolone
‡Ceased Therapy 21 September, 1974

Comment

A history of central myalgia, elevated sedimentation rate and symptomatic relief from steroids was the key to a diagnosis of polymyalgia rheumatica and biopsy proven arteritis.

Case 20

The patient was hospitalized May 2, 1974 after suffering multiple bruises in a fall. The sedimentation rate was found to be 77 mm. and 93 mm. on May 6, 1974. Four months later, she experienced her first girdle myalgia which brought her to the hospital. Sedimentation rate was 94 mm. On the 2nd hospital day she suffered a hemiparesis. Eighty mg. of Prednisone daily decreased the sedimentation rate to 8 mm. Myalgia quickly disappeared but the hemiparesis improved only in part.

Case 23

The patient had a routine office examination on December 6, 1974. There were no specific complaints or abnormal physical findings. The sedimentation rate was 83 mm. Two months later however, she became aware of interscapular and shoulder myalgia. The sedimentation rate was 71 mm. and decreased to 27 ten days after starting 30 mg. of Prednisone daily.

Comment

Cases 20 and 23 illustrate sedimentation rate elevation preceding the symptoms of polymyalgia by four months and two months. There were no other cases of an unusual sedimentation rate elevation prior to myalgia in the cases reviewed (Table 3). We might have prevented hemiparesis in Case 20 had the disease been recognized in time. In an individual with an elevated sedimentation rate from unknown causes, polymyalgia rheumatica should be considered.

Erythrocyte Sedimentation Rate

Elevation of the sedimentation rate is the most characteristic laboratory finding in polymyalgia rheumatica. The high sedimentation rate has been termed the single most useful laboratory test[6] and only repeatedly observed abnormality.[7] With corticosteroid therapy, the sedimentation rate usually returns to normal in about ten days.[2,8,9] The rapid improvement in the sedimentation rate with steroid therapy can be considered a diagnostic test for polymyalgia rheumatica.[2]

Steroids should be administered in a dosage sufficient to control the symptoms of myalgia and

TABLE 3
The Erythrocyte Sedimentation Rate in Millimeters Per Hour Before Myalgia, at Height of Myalgia and After Steroid Therapy

	Pre-Myalgia	ESR	Myalgia	ESR	Date and Daily Dose of Prednisone Therapy		Post-Therapy	ESR
1	None		15 Nov 55	53*	15 Nov 55	20 mg†	01 Dec 55	30*
2	27 Jan 56	46	30 Sep 59	100	01 Oct 59	2.25 mg‡	05 Nov 59	69
	11 Apr 61	23*	05 Jun 74	63	05 Jun 74	20 mg	09 Jul 74	26
3	None		05 Aug 60	108	None		None	
4	11 Dec 59	20*	21 Jan 64	110				
			13 Jan 65	78	20 Jan 65	40 mg	27 Jan 65	30
5	01 Mar 51	25*	06 May 65	108	14 Nov 66	20 mg	06 Feb 67	37
6	Dec 63	25	24 Aug 65	88	25 Aug 65	20 mg	15 Sep 65	24
7	None		17 Nov 65	78	19 Nov 65	60 mg	24 Nov 65	16
8	None		Jul 66	109	Jul 66	20 mg	Aug 66	9
9	17 Sep 65	20	30 Sep 66	80	30 Sep 66	20 mg	19 Oct 66	19
10	None		30 Jun 61	91	05 Jul 67	20 mg	08 Sep 67	58
11	None		02 Oct 67	57	04 Oct 67	20 mg	27 Oct 67	24
12	None		14 May 69	89	19 May 69	40 mg	06 Jun 69	28
13	11 Oct 62	29	30 Mar 70	58	30 Mar 70	20 mg	01 May 70	16
14	24 Mar 71	31	17 Aug 71	95	17 Aug 71	80 mg	09 Sep 71	28
15	None		05 Dec 71	71	05 Dec 71	60 mg	05 Jan 72	27
16	18 Jun 71	46	26 Jan 72	90	26 Jan 72	20 mg	10 Oct 72	47
17	07 Sep 72	31	26 Jul 73	98	26 Jul 73	30 mg	14 Aug 73	26
18	27 Apr 71	43	30 Oct 73	104	01 Nov 73	30 mg	21 Nov 73	27
19	15 May 73	27	30 Nov 73	100	30 Nov 73	30 mg	10 Dec 73	45
20	16 Mar 74	31	16 Sep 74	94	17 Sep 74	80 mg	20 Sep 74	70
	03 May 74	77					24 Sep 74	31
	06 May 74	93					01 Oct 74	8
21	24 Jul 72	22	20 Dec 74	98	27 Dec 74	60 mg	02 Jan 75	31
22	None		08 Jan 75	82	12 Jan 75	30 mg	30 Jan 75	16
23	07 Aug 73	39						
	06 Dec 74	83	14 Feb 75	71	14 Feb 75	30 mg	24 Feb 75	27
24	14 Mar 73	26	26 Feb 75	112	26 Feb 75	-30 mg	12 Mar 75	37

*Wintrobe, others Westergren
†Prednisolone
‡Dexamethasone

maintain the sedimentation rate at a near-normal value. The disease is self-limited and said to last two to four years, although we have continued to use low-dose steroids up to 10 years to control the muscular discomfort and sedimentation rate.

Temporal Artery Biopsy

Biopsies of the temporal artery show arteritis in about one-half of the cases of polymyalgia rheumatica.[2,3,4] Although steroid therapy was recommended for biopsy positive individuals in the past,[4,5] it is now apparent that because of "skip areas"[10,11] a negative biopsy does not preclude the diagnosis.[3] In most clinical settings of polymyalgia rheumatica, we have considered the diagnosis established if there was prompt improvement in the myalgia and a drop in sedimentation rate upon adrenocorticosteroid therapy.

Complications

Complications of polymyalgia rheumatica are related to vascular disease. Usually they involve the eye but can produce cerebral, coronary, renal or peripheral vascular insufficiency. Ocular complications, usually unilateral blindness, occurred in 13 of 212 reviewed cases of polymyalgia rheumatica.[3] Bilateral blindness was found in 17% of patients with temporal arteritis in a pre-steroid group and in 9% of those treated with steroids.[12]

Our experience suggests that prompt recognition and therapy of the polymyalgic syndrome will markedly decrease ocular and other ischemic complications. There has been no blindness in our last 15 patients.

Summary

Twenty-four cases of polymyalgia rheumatica are reported. Erythrocyte sedimentation rate is the most important diagnostic test. In two instances, sedimentation rate elevation preceded the symptoms of myalgia. A case of recurrent polymyalgia rheumatica with a 14 year symptom-free interval is reported. With a diagnosis of polymyalgia rheumatica or giant cell arteritis, Prednisone therapy should be used in a dosage sufficient to control the symptoms of myalgia and maintain the sedimentation rate at or near-normal.

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Continuing Medical Education

Annual Headwater's Clinical Conference

"Nonmalignant Disease of the Colon and Rectum" is the title of the annual Headwater's Clinical Conference to be held Friday, June 18, 1976 at Bemidji, Minnesota. For registration information, contact J. T. Deweese, M.D., Bemidji Clinic, Bemidji, Minnesota 56601.

Annual Meeting—Rochester—May 20 & 21

Remember the fun we had at last year's Bavarian Beer Fest? We're planning another great, relaxing event for the finishing touch to CME '76. On Friday, May 21 at 4:30 p.m., plan on joining in the activities of the Riverboat Jazz Seminar. The fabulous Turkey River All Star Band will entertain us with their festive tunes. Please join us at the Kahler Hotel, Poolside, on Friday, May 21!!!

Anti-i Hemolytic Anemia in Infectious Mononucleosis

JAMES A. WALKER, M.D.* and PAUL B. DICKINSON, M.D., F.A.C.P.*

A 21-year-old man with infectious mononucleosis developed severe jaundice (total bilirubin 15.0 mg%). Since liver involvement in infectious mono is mild (bilirubin usually less than 4 mg%), further laboratory testing was done to elucidate the cause of the jaundice. The patient was found to be anemic with positive direct and indirect Coombs and a cold agglutinin titer of 1:896. Antibody screening revealed that the patient had an IgM anti-i hemolytic anemia. The patient recovered within a week and did not require steroids.

MILD JAUNDICE OCCASIONALLY OCCURS in infectious mononucleosis. Severe jaundice should alert the clinician to suspect a hemolytic anemia rather than severe hepatocellular disease. We report here a case of infectious mononucleosis complicated by jaundice secondary to hemolytic anemia due to anti-i antibodies.

Case Report

A 21-year-old white man sought medical advice for fever and upper respiratory symptoms. SMA-12, WBC and mono spot were all normal. Symptoms persisted, and he was seen in the Bethesda outpatient department on November 26, 1974. He complained of throat pain, rhinorrhea, fever, and vomiting. He was treated with oral penicillin. Two days later he became jaundiced and was admitted to the hospital. The patient had never received serum or serum products, had never used drugs, and drank alcohol rarely. A younger sister had hepatitis two years earlier.

Physical examination disclosed an acutely ill-appearing jaundiced young man. Temperature was 100°F, BP 110/80, pulse 90. Tender, moderately enlarged lymph nodes were palpable in both the anterior and posterior cervical chains, and the pharynx was injected with a creamy white exudate. The liver area was tender to percussion, but neither the liver nor the spleen was palpable.

Laboratory findings included: Hgb 14.5, WBC 6300 with 52% PMN's, 11% stabs, 38% lymphs, and 1% basophils. Atypical lymphs were present. Urinalysis showed bilirubin, and the urobilinogen was 12 Ehrlich units. Total serum bilirubin was 13.8 mg% with direct bilirubin 8.7 mg%. SGOT was 180.

Other studies done included hepatitis B antigen, rheumatoid factor, VDRL, red cell fragility and PNH screen all of which were normal. Mono spot tests on 11/28 and 12/2 were positive.

Course

Soon after admission the patient's symptoms improved. However, on 12/1/74, his hemoglobin dropped to 11.5 gm%. A peripheral smear showed a normochromic, normocytic anemia. Cold agglutinins were positive at 1:896. Direct Coombs was weakly positive. Indirect Coombs was also positive and antibody screening revealed both auto-anti-I, and anti-i. The anti-i proved to be an IgM immunoglobulin. His hemoglobin dropped to a low of 9.2 gm%. Steroid therapy was not required, and he was discharged on 12/9/74. He was asymptomatic when seen on 12/16/74, his hemoglobin then was 12.8 gm%.

Discussion

This patient had hepatic involvement as evidenced by elevated SGOT and LDH. Hepatic involvement is seen in 80-90 percent of patients with mononucleosis. In fact, Evans lists hepatic dysfunction as a criterion for diagnosing infectious mononucleosis.[1] Liver involvement is usually mild, and the bilirubin rarely exceeds 4 mg%[2] The

TABLE

TEST		11/28	11/29	11/30	12/1	12/2	12/3	12/4	12/5	12/6	12/7	12/8	12/9
Bilirubin,	Direct	8.7			9.0		2.2			1.0		1.1	
	Total	13.8			15.0		3.8			2.4		2.0	
SGOT		180			561		281			112		86	
LDH					808		408			322			
Alk. p'tase					107		115			108			
Hgb		14.5		11.5		9.7	9.2	9.3	9.7	9.8	9.8	10.7	12.8
Retics						7.3	8.0	15.1	13.7			25.5	
PT/C					19.4	16.0						15.4	
					14.4	13.9						13.9	

---

*Department of Family Practice and Digestive Disease Laboratory, Bethesda Lutheran Hospital, St. Paul, Minnesota.

See editorial, page 317.

hepatic dysfunction does not reflect direct hepatocellular injury but damage to the liver reticuloendothelial system. Chronic active liver disease or cirrhosis does not occur as a sequelae of mononucleosis.[3,4]

Hemolytic Anemia

A mild hemolytic anemia occurs in three percent of patients with infectious mononucleosis. This hemolysis is caused by anti-i antibodies.[2] Weiner discovered the existence of an Ii blood cell antigenic system in 1956 in a patient with acquired hemolytic anemia of the cold antibody type.[5]

Subsequent studies have shown i antigen is present in high titers in fetal red cells and is gradually replaced by I so that by 18 months of age, the I antigen predominates. However, even in adults, there are minimal amounts of i antigen present and in a small number of adults (less than 0.1%), the fetal form of cells containing primarily the i antigen is retained. The Ii antigens are found on red cells, white cells and platelets.

Anti-i

Anti-i is most likely a cold agglutinin of the IgM class. IgM levels in infectious mononucleosis are increased 100 percent, but only five percent of the increase is due to the heterophil antibody.[2] Anti-i is one of many IgM immunoglobins found in patients with mononucleosis. It has also been found in reticulum cell sarcoma, alcoholic cirrhosis, malaria, ulcerative colitis, lymphocytic leukemia, myelofibrosis, metastatic carcinoma, pregnancy, and even in normal people.

Anti-i antibody will agglutinate fetal red cells and those adult red cells with primarily i antigen. It will also agglutinate normal red cells if the titer of anti-i is high enough. This probably happens because of the small amount of i still present in adult red cells. Anti-i generally appears during the first week of infectious mononucleosis before the patient is heterophil positive. Anti-i- disappears before the heterophil and its disappearance is commensurate with clinical and hematologic recovery even if the heterophil is still positive.

Positive Direct Coombs

A positive direct Coombs generally indicates IgG antibody so use of standard Coombs serum may fail to detect the IgM anti-i.[5] Thus, in suspected cases it is important to use Coombs serum with anticomplement activity as well as anti-IgG activity. It is the non-γ component (anti-complement) which causes visible agglutination by reaction not with the cold antibody coating the cell but the complement which binds the cold antibody to the cell. Therefore, the frequent negative direct Coombs in reported cases of mononucleosis complicated by hemolytic anemia may reflect absence of anti-complement in the Coombs serum used.

Previous Study

Deaton (1967) reviewed 38 cases of hemolytic anemia associated with infectious mononucleosis.[6] In 73 percent, the lowest hemoglobin was less than 8 gm%. Twenty-four percent had hemoglobinuria, 56 percent had a positive direct Coombs, and 65 percent had a cold agglutinin titer greater than 1:64. The course was generally that of a severe but transient illness with spontaneous recovery in a few weeks. However, transfusions or steroids were required in one-third of the reported cases. Recent studies including those of Rosenfield (26/38), Calvo (23/38), and Wolheim (27/36), indicate that about two-thirds of patients with infectious mono have anti-i in low titers without overt hemolysis.[5] Hossaini found that 69 percent of 52 patients had anti-i.[7] He retested twelve patients four to six weeks after the onset of mono, and all were negative. Anti-i can be demonstrated in two-thirds of patients with infectious mononucleosis, but only three percent have overt hemolysis.

Acknowledgments

Characterization of the anti-i antibody was performed by Dr. Manuel Kaplan at the Minneapolis Veteran's Hospital. Drs. Robert J. Johnson and Delbert Nelson of the Rice Street Clinic were the primary physicians involved in this patient's care.

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Human Myiasis by the Black Blow Fly

Brief Clinical and Laboratory Observations of Three Cases

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Observations of three cases of human myiasis, two aural and one of the scalp, due to Phormia regina (black blow fly) are presented.

MYIASIS IS THE invasion of tissues or organs of living humans or animals by maggots, the larval stages of flies. James and Harwood[1] reviewed the subject in general, listing types of myiasis and specific flies and hosts involved. Some of the myiases, in the North Central states area involving humans, recently published include Tumbu-fly myiasis,[2] and flesh-fly myiasis.[3-5] Stuart[6] in 1929 described a case of myiasis due to the black blow fly in a 25-year-old woman in Texas. Her scalp infection produced an extremely offensive odor and this odor was believed to have attracted the ovipositing fly or flies to the wound, resulting shortly in masses of living larvae within the tissues at that site. Cunningham and Zanga[7] described a case of aural myiasis in a seven-week-old infant with no history of trauma, previous infection, or fever. The parents kept three monkeys as pets which attracted many flies to them, and thus to the child's immediate environment. Six actively moving larvae were removed from the ear canal, and subsequently identified as those of the blow fly (family Calliphoridae).

Myiasis due to blow flies is considered uncommon in man. This report presents three documented cases of black blow fly myiasis in Minnesota in one year.

Case Reports

Case 1

On July 18, 1974 a 70-year-old man in Bagley, Minnesota felt a fly lighting on his left ear and instantly brushed it away. Two days later he presented himself to the clinic with complaints involving the left ear. The physician recovered 30 to 50 larvae in the ear washings. Later that day the patient returned complaining of further annoyance in the ear, and the physician again examined the ear. He noted a perforation in the ear drum and saw two larvae moving about in the middle ear. He placed mineral oil in the ear, and the patient returned to the clinic the next morning. One of the larvae had crawled out of the middle ear space and was in the ear canal. It was removed leaving the remaining one in the middle ear. The following day (48 hours after the initial clinic visit) the patient again was examined. The remaining larva was at the perforation and was readily removed, using a suction tip.

Case 2

In July 1975, a 56-year-old Wisconsin man, while camping in the woods near Duluth, Minnesota, felt a fly enter his right ear. His wife later that day examined his ear, and she was unable at that time to see anything in the ear. Approximately 10 days later the man experienced pain and bleeding from the right ear and stated that he could feel something crawling in the ear. On examination his ear was found to be filled with approximately 50 to 60 larvae. These were removed using suction, and further inspection of the ear under the operating microscope revealed a small perforation in the tympanic membrane. The surface of the tympanic membrane was completely denuded of epithelium. No larvae could be seen in the middle ear, through the perforation, but the middle ear mucosa was thickened and edematous in appearance. Because the patient continued to experience some pain in the right ear, an exploratory tympanotomy was performed on August 28, 1975. The findings at the time of operation consisted of thickened mucosa with adhesions in the area of the stapes. The ossicles were intact, and no evidence was found of cholesteatoma or of larvae.

Case 3

A 55-year-old woman in Excelsior, Minnesota had been aware for several months of a lump developing on her scalp. On August 23, 1975 the lump apparently began draining blood. She presented herself at the physician's

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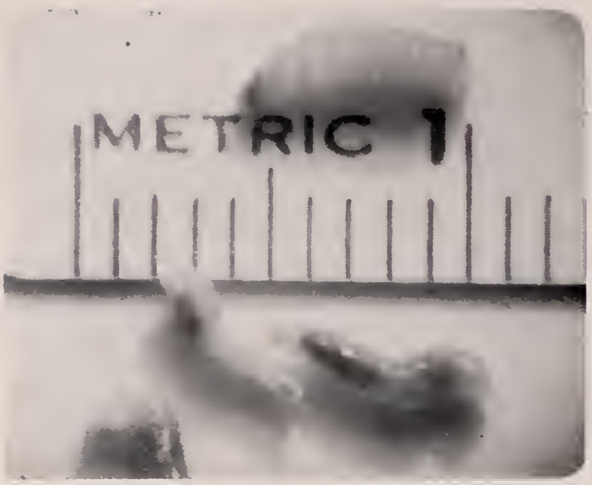

Fig. 1—(Above) Mature larva from Case 1. (Below) Immature larvae from Case 2. Each scale division equals 1 mm. (X5)

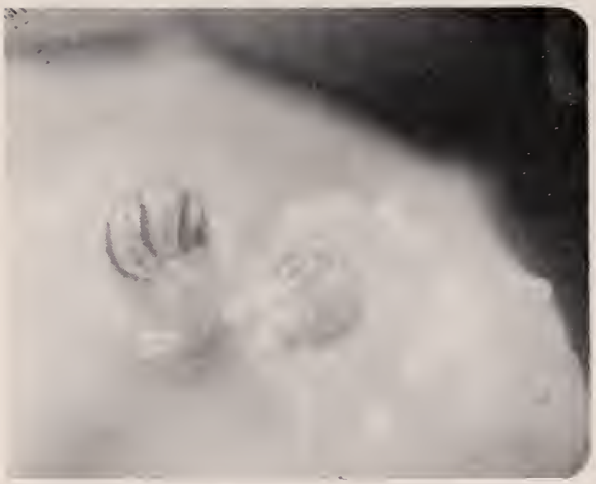

Fig. 2—Posterior spiracles on an immature larva from Case 2. (X200).

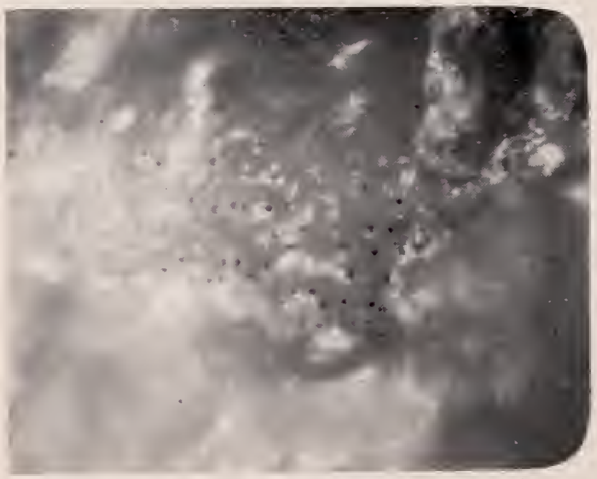

Fig. 3—Size, shape and arrangement of microspines on an abdominal segment of an immature larva from Case 3. (X270)

office requesting examination of the growth. Examination showed a 3 cm. mass on the right parietal region which originally might have started as an epidermoid cyst. It was infected, open, and teeming with maggots—at least 50.

The mass was unroofed, and the maggots were removed. The base of the lesion was bloody and appeared to be chronically infected. Furacin cream was applied, and the wound was dressed. The patient was examined again on August 25 and one maggot found. The patient was instructed in wound care and told to return in one week. On the return visit more necrotic tissue was found in the wound. It was totally excised to clean out the area. A frozen section suggested a low grade squamous carcinoma. Permanent tissue sections showed severe dyskeratosis. The scalp lesions at this writing are completely healed.

About a dozen larvae from each documented case have been submitted to the Division of Medical Laboratories, Minnesota Department of Health for identification. All larvae were fairly uniform in size, regardless of maturity (Figure 1), and by use of identification keys,[8,9] the immature larvae were identified. The characteristics of the posterior spiracles (Figure 2) are extremely important in the identification of the species of fly. Since all submitted larvae except one were immature, however, not all identifying structures were consistent with those of mature larvae presented in the identification key[8] and examination of the microspines[9] (Figure 3) was necessary for additional evidence of the correct species designation.

Each posterior spiracle on the mature larva examined showed an incomplete, thin peritreme which had no projections. Inside each peritreme were three distinct slits. These slits were straight, not sinuous, they had no lateral swellings, and they pointed toward the opening in the peritreme. The immature larvae examined showed only two slits but were identical in all other spiracle characteristics described for the mature larva.

Bands of black bifurcate-appearing microspines, on each segment of the larvae, showed, characteristic for this specie, large, isolated, randomly arranged spines, progressing caudally to successively smaller spines which are successively closer together and in orderly horizontal rows.

Discussion

In addition to myiasis, the blow fly, a scavenger, has been incriminated as a mechanical vector of agents of bacillary enteritis in man. It produces myiasis in sheep and cattle in the Southwestern United States where it is found in incision wounds of the castrated or dehorned animal.[10] These wounds provide a place for the blow fly to deposit eggs and larvae to develop. In the human, exposed wounds and orifices[11] such as the external ear canal, are sites of oviposit by this fly. The hatched maggots produce traumatic damage to the immediate tissue.

In Case 3, myiasis of the scalp, the foul odor probably was the attractant for the fly searching for a suitable substrate on which to oviposit. In the two cases of aural myiasis, however, there were no pre-existing wounds, and no known circumstances which may have lured these flies to the immediate environment of the patients. What attracted the fly to the ear in each case is a matter of speculation.

How prevalent human myiasis is in Minnesota and which flies are involved are not known since myiasis is not reportable to the Minnesota Department of Health. One of the functions of the Health Department is the gathering of public health data, assembling, and presenting the information to the medical community.*

Acknowledgment

For assistance in identifying the immature larvae in Case 1, the authors are grateful to Mr. John Luhman and Mr. David Noetzel, Extension Entomology, University of Minnesota, St. Paul, Minnesota.

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*We ask for the cooperation of physicians who encounter myiasis cases: they should submit specimens of the larvae to the Division of Medical Laboratories, Minnesota Department of Health, along with data on the patient involved.

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Dr. Konald Prem Named OB-Gyn Head at U of M

Dr. Konald Prem has been named professor and head of the department of obstetrics and gynecology at the University of Minnesota.

Dr. Prem received his M.D. degree from the University's Medical School in 1951. He joined the department faculty in 1955 and has been director of gynecologic oncology since 1969.

His medical education was earned from the University of Minnesota, and since 1951 he has had many University appointments in the Department of Obstetrics and Gynecology, including: medical fellow, instructor, associate professor, professor and director, gynecologic oncology, up to the present appointment as Professor and Head of the Department. He has been certified by the American Board of Obstetrics and Gynecology with Special Competence in Gynecologic Oncology, and has numerous memberships in professional and academic societies. The list of his guest lectureships is long and impressive as the special honors bestowed on him by various medical groups.

In 1974 Dr. Prem was promoted to Brigadier General in the United States Army Medical Corps Reserve. Currently he is commander of the 5501 U.S. Army Hospital at Fort Snelling with units in Minnesota and Iowa. The Board of Editors of Minnesota Medicine is very proud that Dr. Konald Prem is an Associate Editor of the Journal, a position he has held since 1961.

A.M.A. President, Dr. Max H. Parrott will be there . . . Minnesota Physician and Educator, Dr. Robert W. tenBensel will be there . . . Dr. H. William Scott, Jr., President of the American College of Surgeons will be there . . . May we count on you? C.M.E. '76, May 20-21, Rochester.

Causes of Death of Institutionalized Phenylketonuric (PKU) Patients-A National Survey

ROBERT O. FISCH, M.D.,* MARY K. BILEK, M.S.,† and HEINZ H. BRUHL, M.D.‡

A national survey of state institutions for the mentally retarded was undertaken to determine the age at the time of death, the sex distribution, and the primary and secondary causes of the deaths of phenylketonuric inmates, as well as to discover whether there was a possible protective mechanism against certain diseases and death in cases of phenylketonuria. The survey revealed that the sex distribution was equal, and that more than 50% of the phenylketonuric inmates died under 27 years of age. Difficulties in feeding and management were the most frequent factors leading to death, but the phenylketonuric inmates were not spared any known causes of death. The amino acid imbalance does not seem to be a protection against infection, cardiac complications or malignancies.

LITTLE INFORMATION is available about institutionalized phenylketonurics.[1,2] The pathological findings about phenylketonuric patients are restricted chiefly to the neuropathological changes within the brain, and refer only grossly to other causes in a few isolated cases.[3-9] The most common pathological conditions described in phenylketonuria are the reduction of brain weight, myelinic alterations, glia hyperplasia, and hypopigmentation of the substantia negra.[10] Because of the lack of information, a survey by mail was undertaken to determine the ages, the sex distribution, and the primary and secondary causes of the deaths of phenylketonuric inmates, as well as to discover whether there is a possible protective mechanism against certain diseases or causes of death in cases of phenylketonuria.

Methods and Materials

The addresses of the superintendents or medical directors of 266 state institutions in the United States were obtained from a list compiled in 1973. They were each sent a letter with a questionnaire soliciting information about: (1) the number of diagnosed phenylketonurics in their institutions since 1950;‡ (2) the number of phenylketonurics who have died since 1950; (3) their sex, birthdate, and age at the time of death; (4) their highest recorded serum phenylalanine level; (5) the presence or the absence of phenylketones in their urine; (6) the autopsy report giving cause of death as well as additional pathological findings; and (7), in the absence of an autopsy, the diagnosed cause of death and previously established diagnostic conditions contributing to death.

The letters and questionnaires were sent out on May 17, 1974. We received 210 replies (79%) by September, 1974.

The 210 institutions reported a total of 1603 phenylketonurics from 1950 to the time of the report. Of the 172 who died during that period, 79 were male, 79 were female, and 14 of unspecified sex. In 77 of the 172 cases, autopsies were performed, and in at least 80 cases they were omitted. (There is no information about the remaining 15 cases.) Recorded serum phenylalanine levels were over 20 mg.% in most decedents, with the exception of 13 cases in which they were between 15 and 20 mg.% In the two patients with phenylketonuria who were on a low phenylalanine diet, the serum phenylalanine levels were below 10 mg.%.

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‡This year was picked as an arbitrary and convenient cutoff date. It is our educated guess that previous to this date, state institutions kept even fewer records pertaining to phenylketonuric patients than they did thereafter.

Phenylketones in the urine were found in 110 cases; their presence or absence was not reported in the remaining cases.

The age of death varied from seven years to 87 years of age.

The age distribution of the deceased males and females is presented in Table 1, which indicates a very high incidence of early death for phenylketonuric inmates. More than 50% died under 27 years of age.

Causes of Death

The primary causes of death in the majority of cases are listed in Table 2. Among them are pneumonia (mostly aspiration); cardiovascular abnormalities; gastrointestinal complications; malignancies (intraventricular glioma, Hodgkin's Disease, disseminated cancer, carcinoma of the stomach with generalized metastasis, reticulum sarcoma, malignant melanoma with regional lymphatic involvement, bronchogenic adenosarcoma of the lung, testicular seminoma with metastasis, lymphosarcoma), kidney abnormalities, etc. The secondary causes are listed in Table 3. Among them are infections as well as pathological changes in the lungs, kidney, stomach, and intestines.

Discussion

Our survey confirmed the previous observation[2] that institutionalized untreated phenylketonurics die at a generally early age. This finding suggests that the life expectancy of the untreated phenylketonurics may be considerably lower than that of the normal population, and that the most frequent immediate causes (aspiration, pneumonia, and gastrointestinal complications) of death may be aggravated or sometimes initiated by difficulties in feeding and managing such severely re-

TABLE I
Death by Age and Sex of PKU Patients

Age at Death (years)	Male Number	Male %	Male Cum. %*	Female Number	Female %	Female Cum. %	Total Number	Total %	Total Cum. %
<10	1	1	1	3	4	4	4	2	2
10-19	19	24	25	20	25	29	39	25	27
20-29	24	30	55	19	24	53	43	27	54
30-39	15	19	74	11	14	67	26	17	71
40-49	7	9	83	7	9	76	14	9	80
50-59	3	4	87	6	8	84	9	6	86
60-69	6	8	95	10	13	97	16	10	96
≥70	4	5	100	3	4	101	7	4	100
Total	79	100		79	101		168	100	

Cum. %: Cumulative Percentage

TABLE 2
Primary Causes of PKU Deaths

Lung (75)	
Bronchopneumonia	52
Aspiration Pneumonia	15
Bacterial & Viral Pneumonia	4
Lung Abscess	2
Pulmonary Edema	1
Respiratory Arrest	1
Heart (23)	
Heart Failure	8
Myocardial Fibrillation	2
Cardiorespiratory Failure	2
Coronary Occlusion	5
Cardiac Arrest	2
Cardiovascular Hypertension	1
Congenital Heart Defect	1
Arteriosclerotic Heart Disease	1
Thromboemboli, left atrium	1
Abdomen (17)	
Gastric Hemorrhage	6
Perforated Ulcer	2
Peritonitis	4
Chronic Colitis	1
Ileus Infarction	4
Cancer (9)	
Intraventricular Glioma	1
Hodgkin's Disease	1
Disseminated Cancer	1
Carcinoma of Stomach with Metastasis	1
Reticulum Sarcoma	1
Melanoma with Reginal Lymphatic Involvement	1
Adenocarcinoma	1
Testicular Seminoma	1
Lymphosarcoma	1
Malnutrition (8)	8
Brain (6)	
Cerebral Vascular Accident	2
Status Epilepticus	4
Kidney (6)	
Renal Failure	6
Others (10)	
Accident	2
Meningoencephalitis	1
Sepsis	3
Shock	4

TABLE 3
Secondary Causes (Diagnoses) of PKU Deaths

Lung	27	
Emphysema		2
Empyema		7
Bronchitis-chronic		1
Atelectasis		2
Fistula		1
Pleuritis		1
Hemi Thorax		1
Hydro Thorax		1
Tuberculosis		5
Pulmonary Edema		4
Pulmonary Fibrosis		2
a. Pneumonia	15	
Bronchopneumonia		9
Aspiration Pneumonia		1
Bacterial Pneumonia		1
Viral Pneumonia		1
Hypostatic Pneumonia		2
Asphyxia		1
Heart	17	
Myocarditis Viral		4
Heart Failure		6
Coronary Sclerosis		1
Coronary Occlusion		3
Hypertension		2
Congenital Heart Defect		1
Abdomen	25	
Colon Infarction		1
Perforated Ulcer		1
Peptic Ulcer of Duodeum		1
Perforation-Gastric Ileus		3
Intestinal Volvulus		2
Infarction-Intestine		2
Bowel Obstruction		6
Gastric Hemorrhage		2
Cholelithiasis		1
Hirschprong's Disease		1
Ovarian Cyst		1
Enteritis		1
Cirrhosis		1
Hiatus Hernia		1
Peritonitis		1
Central Nervous System	25	
Hydrocephelus		1
Cerebral Edema		1
Brain Degeneration		10
Cerebral Arteriosclerosis		1
Triplegia		1
Spastic Quadriplegia		3
Cerebral Palsy		2
Epilepsy		6
Malnutrition (8)	8	8
Kidney (11)	11	
Atrophy		3
Nephritis		2
Pyelonephritis		2
Chronic Glomerulonephritis		2
Uremia		1
Pyelolithiasis		1
Others (5)		
Kyphoscoliosis		1
Hyperplasis Thyroid		1
Anemia		2
Esophagogastritis		1

tarded individuals. It is hoped that compulsory screening and early dietary restriction for phenylketonuria will reduce the number of institutionalized retarded phenylketonurics[11] who are difficult to manage and thus die early in life.

The hereditary transmission of phenylketonuria independently of sex was established by Jervis,[1] although proportionately more male than female phenylketonurics have been found in the screening program.[12] This finding has been attributed to the fact that in the first four days of life, the blood phenylalanine concentration is higher in male phenylketonurics than in female phenylketonurics.[13]

The amino acid imbalance of phenylketonuria was first described by Bickel and Hall,[14] whose description was later restated by others.[15-17] The toxic effect of chloromphenical on bone marrow can be reversed by the short-term ingestion of phenylalanine doses.[18] Similar bone marrow changes observed in phenylketonurics on a low-phenylalanine diet were likewise reversible by the addition of phenylalanine to the diet.[19] Phenylalanine inhibited the antibacterial effect of chloromphenicol *in vitro*.[20] Among untreated phenylketonurics, the following conditions were observed: lipid composition abnormalities;[21,22] decrease in the synthesis and increased utilization of acetyl coenzyme A; and decreased production of cholesterol.[23] The deliberate inducement of an amino acid imbalance by adding L-phenylalanine and tyrosine to the normal diet has been used for the treatment of leukemia.[24] This measure has also been recommended for the treatment of malignancies.[25,26]

Difficulty in feeding and managing the phenylketonurics in this survey aggravated or possibly even initiated the primary and secondary causes of their deaths in most cases; similar difficulties of feeding and management are not unique to PKU patients, but common to most other patients who require institutionalization. Thus the most probable cause of death resulting from phenylketonuria cannot be established from a survey of this highly selected population. Although many of the phenylketonuric inmates died early in life, they had a high incidence of infections and malignancies. The infections were localized bacterial infections of the lungs, septicemia, peritonitis, and other unidentified viral infections. Thus, phenylketonurics are not protected from malignancy, and the incidence of death due to malignancy would presumably increase if many of these institutionalized phenylketonurics did not die early in life.

The mortality statistics of the early treated phenylketonurics with normal intelligence must be studied in order to establish the life expectancy and the probable cause of death of phenylketonurics.

Acknowledgment

The authors wish to thank all the superintendents and medical directors of the institutions for their cooperation. We also express our thanks to Mrs. Jean Marquardt for her assistance in the preparation of the data.

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Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

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Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I. reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

Supplied: Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

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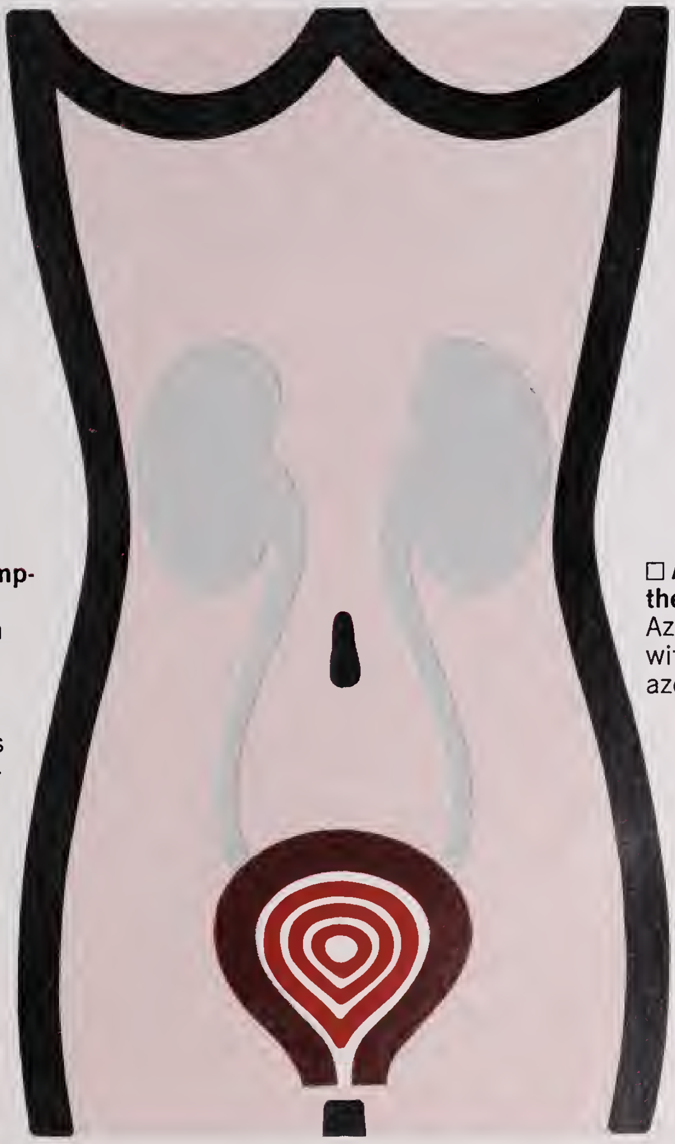

☐ **Early relief of painful symptoms** such as burning and discomfort associated with urgency and frequency.

☐ **Effective control of susceptible pathogens** such as *E. coli*, *Klebsiella-Aerobacter*, *Staph. aureus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*.

☐ **Appropriate antibacterial therapy:** up to three days with Azo Gantanol, then 11 days with Gantanol® (sulfamethoxazole).

*nonobstructed; due to susceptible organisms

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FOR LONG-TERM CONTROL OF HYPERTENSION*

Serum K+ and BUN should be checked periodically. (See Warnings Section.)

SPARES POTASSIUM

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

> *Warning
> This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

*Indications: *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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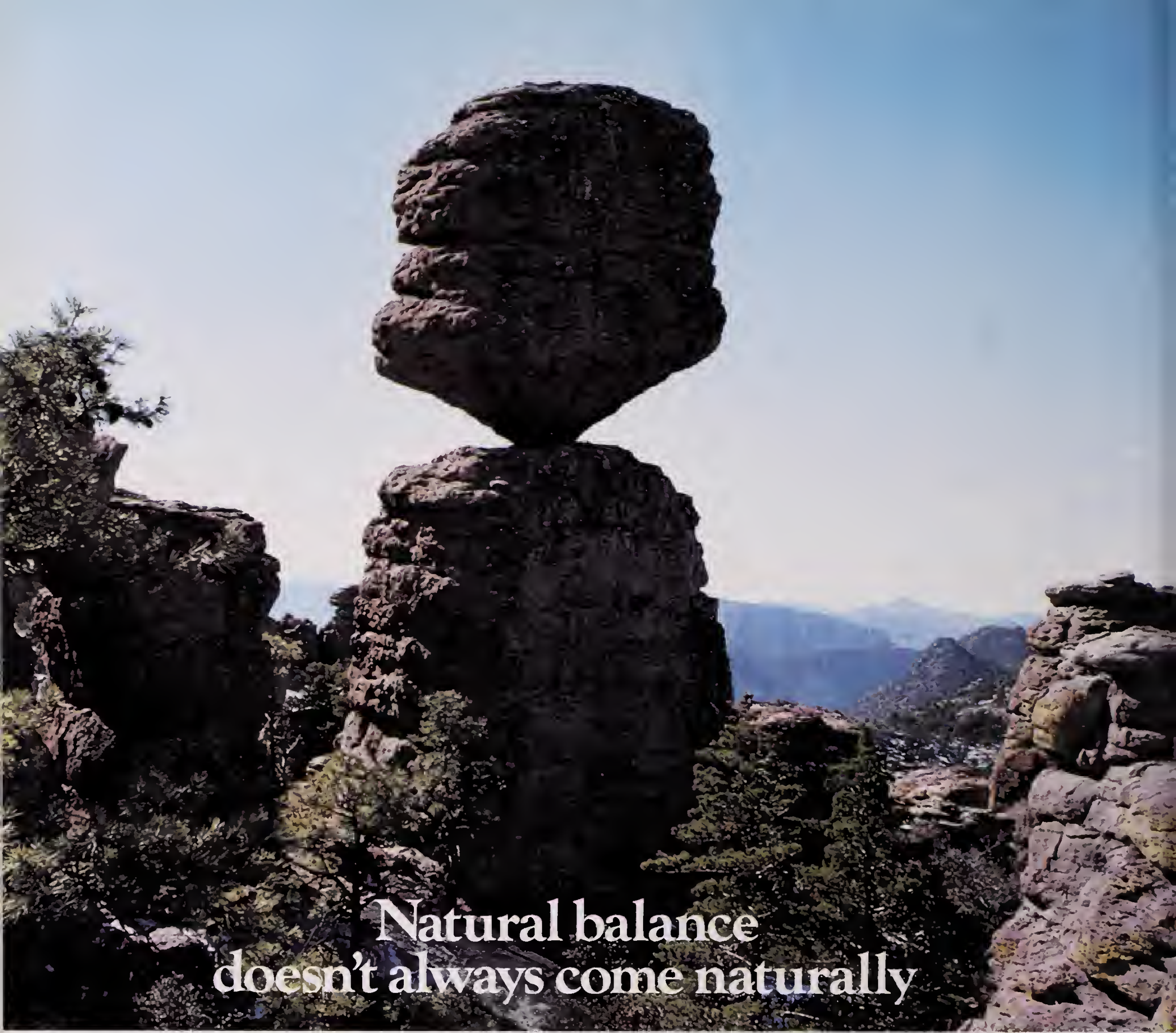

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☐ Found useful in the management of vertigo* associated with diseases affecting the vestibular system.

☐ Can relieve nausea and vomiting often associated with vertigo.*

☐ Usual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.

☐ Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.

☐ Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during preg- nancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurre vision have been reported.

More detailed professional information available on request.

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Antivert®/25
(meclizine HCl) 25 mg. Tablets
for vertigo*

Editorials

Hepatitis B

THE DETAILED REPORT by Bruhl and Associates* in the April issue of MINNESOTA MEDICINE shows again, how many problems remain to be solved around infectious hepatitis. Their study confirms previous reports about the relatively high prevalence of hepatitis B virus among patients in institutions for the mentally retarded. Their finding that a higher rate of antigenemia is observed among non-toilet-trained, ambulatory patients, further supports the assumption that hepatitis B may be transmitted non-parenterally. It is interesting to read in this paper that clinically-recognized hepatitis B occurred approximately as often in patients as in hospital employees. I wonder how often antigenemia is found in personnel, as none of 55 patients who were hepatitis B surface antigen (HB_sAg) positive showed clinical evidence for hepatitis. Maybe in these employees, the carrier rate is rather high as well.

A solution in this puzzle might come if a study like this would also apply newer tests such as for e antigen and anti-e, as recently described.[1,2] Here, a significant association of anti-e with a normal or only mildly abnormal liver was found in HB_sAg carriers, while e antigen was associated with active and usually continuing liver disease. The e antigen system is different from HB_sAg but only present in HB_sAg-positive patients.

Using immunofluorescence, it could be shown recently,[3] that two different patterns of IgG are seen on hepatocyte membranes of patients with hepatitis: a linear pattern was found in HB_sAg-negative hepatitis, whereas HB_sAg-positive patients had a granular pattern, but "healthy" HB_sAg carriers did not show this granular pattern. This points to the possible role played by an autoimmune process in chronic active hepatitis.

I agree with the authors' and others'[4] conclusion that HB_sAg positivity alone does, in itself, not seem to present a particularly high risk to others if good hygiene is maintained. Furthermore, testing for e and anti-e as well as for liver membrane autoantibody might permit us to prognosticate even more accurately for patients or carriers with HB_sAg. Much remains to be done, especially as there is not yet any treatment for hepatitis available.

Claus A. Pierach, M.D.
Minneapolis, Minnesota

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*See page 263.

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2. Feinman SV, Berris B, Sinclair JC et al: e antigen and anti-e in HB_sAg carriers. Lancet 2:1173, 1975.
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4. Redeker AG: Hepatitis B: Risk of infection from antigen-positive medical personnel and patients. (Editorial) JAMA 233:1061, 1975.

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Disseminated Gonococcal Infection

HEMORRHAGIC PUSTULES are an important diagnostic feature of disseminated gonococcemia. Isolated small vesicles appear in crops and quickly become tender, palpable, hemorrhagic pustules. The extremities, particularly the fingers, are most commonly involved. Fever, arthritis, periostitis, and tenosynovitis are also often present.

Bamford and Bloom recently reported a woman with plasma cell myeloma and disseminated gonococcemia.[1] Although the association of these two diseases may be fortuitous, patients with myeloma have low serum levels of normal immunoglobulins, which may favor dissemination of *N. gonorrheae* organisms. Patients with congentital deficiencies of the late components of complement are also probably more prone to disseminated gonococcemia.

Nonetheless, most patients with disseminated gonococcemia do not have a recognizable acquired or inherited immunodeficiency. The reason why some patients develop septicemia remains unclear, but may result from failure of local tissue defense mechanisms or abundance of pathogenic organisms, or both. Disseminated gonococcemia occurs in ½% to 3% of persons infected with *N. gonorrheae*.[2]

Treatment of disseminated gonococcemia with penicillin is usually curative once the diagnosis is established.[3] Skin lesions are neither pathognomonic nor always present. The diagnosis is best confirmed by isolation of *N. gonorrheae* from urethra, cervix, rectum, pharynx, or blood of infected persons. The organism is usually not demonstrable in tissue sections or smears of skin lesions except by direct immunofluorescence. Bacterial culture of skin biopsy specimens is frequently negative.

Crops of isolated, tender, hemorrhagic vesiculopustules on bright or dusky red bases in a patient with fever may suggest disseminated gonococcemia.

Mark V. Dahl, M.D.*
Minneapolis, Minnesota

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*Assistant Professor of Dermatology, University of Minnesota Medical Center.

References

1. Bamford JTM, Bloom SL: Disseminated gonococcemia in plasma cell myeloma. Minnesota Med 59:4:230, 1976.
2. Shapiro L, Teisch JA, Brownstein MH: Dermatohistopathology of chronic gonococcal sepsis. Arch Derm 107:403, 1973.
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Anti-i Hemolytic Anemia in Infectious Mononucleosis

INFECTIOUS MONONUCLEOSIS has varied presentations and courses. Walker and Dickinson* in their nicely documented article Anti-i Hemolytic Anemia in Infectious Mononucleosis, concentrate on one of the organ systems affected, blood. Hemolytic anemia, as mentioned, occurs only in three percent of cases while up to seventy percent have anti i antibodies.[1] Why does hemolytic anemia occur in only three percent?

Persons suffering from thalassemia and spherocytosis seem to have accelerated hemolysis.

Of interest is the simultaneous liver disease. Cytomegalovirus is very similar to infectious mononucleosis in its presentation and should also be considered in similar cases when the testing for infectious mononucleosis is negative.

Gene Hartmann, M.D.
Minneapolis, Minnesota

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*See page 301.

References

1. Hossaini AA: Anti-i infectious mononucleosis. Amer J Clin Path 53:198, 1970.

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Polymyalgia Rheumatica

Polymyalgia rheumatica is a clinical syndrome characterized by the presence of musculoskeletal aching and stiffness in the proximal portions of the body including the shoulder girdle, pelvic girdle, neck, and torso. The discomfort tends to be most prominent after rest and has the features of "gelling" similar to that seen in patients with rheumatoid arthritis. In various recent series, about 15 to 35% of patients with polymyalgia rheumatica have been shown to have an associated giant cell arteritis. Conversely, about 50% of patients with giant cell arteritis have the polymyalgia rheumatica syndrome. Although the incidence of these conditions is not accurately known, they are certainly not as rare as was once thought. At our clinic, for example, we see between 40 to 50 new patients with giant cell arteritis each year. Experience would suggest that these diseases are somewhat less common in non-Caucasian groups. The cause of the prominent aching and stiffness is uncertain. Some investigators have felt that the symptoms may be related to inflammation of the arteries in painful areas, but solid evidence for this is lacking. Other investigators have suggested that polymyalgia rheumatica is a form of arthritis in which the proximal joints are mainly involved. In recent studies, we have obtained evidence supporting the latter concept. We found that scintiscans with technetium pertechnetate showed increased uptake over symptomatic joints in most patients with polymyalgia rheumatica.[1]

Elsewhere in this issue, Nuessle and co-workers* review their experience with 24 cases of polymyalgia rheumatica and point out reasons for being aware of this syndrome. Early recognition of polymyalgia rheumatica is important because when giant cell arteritis is present proper treatment with corticosteroids can prevent blindness, rupture of the aorta, or narrowing of other large vessels of the upper torso, head or neck. Treatment of patients with polymyalgia rheumatica by nonsteroidal drugs or low doses of corticosteroids when arteritis is not demonstrable also is usually very successful. Nuessle and co-workers' observations that an elevated sedimentation rate may precede symptoms in these conditions is, therefore, very timely, but other causes of increased sedimentation rates must be considered as well.[2]

Gene G. Hunder, M.D.
Rochester, Minnesota

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*See page 297.

References

1. O'Duffy JD, Wahner H, Hunder GG: Unpublished data.
2. Zacharski LR, Kyle RA: Significance of extreme elevation of erythrocyte sedimentation rate. JAMA 202:116, 1967.

Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

1. Preferably an alumnus of the University of Minnesota Medical School.
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Letters to the Editor

Atopic Dermatitis

Dear Editors:

I read with interest the work performed by Dr. Joel Bamford* in an attempt to reproduce the studies that I performed previously.

My purpose in the previous report was to give preliminary results on patch testing with food in atopic dermatitis. Since that time the number of patients has considerably expanded. I would hope soon to be able to collect these new experiences and publish them. Examining this new series will allow a more complete discussion of techniques of testing and treating associated with this diagnostic tool.

In the meantime I appreciate learning about the fine works of Dr. Bamford.

William E. Walsh, M.D.
St. Paul, Minnesota

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*Minnesota Med 59:180, 1976.

Poison Control Center

Dear Editors:

It has recently come to my attention that many physicians in the Twin City area and possibly throughout the state are recommending the administration of salt and water to induce emesis in cases of poisoning in children and adults. These physicians are obviously unaware of the potential lethality of their recommendation.

The literature reveals a number of cases of fatal hypernatremia in children and adults secondary to oral salt and water administration for induction of emesis,[1-5] Considering that salt water, as an emetic, has a low order of effectiveness,[6] probably equivalent to mechanical stimulation of the pharynx, the dangers from its use outweigh any potential benefits. Under no circumstances should salt water be recommended for this purpose.

Syrup of ipecac has been shown to be a safe and effective emetic both as a first aid measure in the home and for use in emergency departments. I would suggest that all parents be instructed to purchase a one ounce bottle of syrup of ipecac when their child first begins to crawl and to keep a bottle in their home until the child reaches school age. The parent should also be instructed not to administer the ipecac until a physician or poison control center has been contacted and the need for emesis has been determined.

The Poison Control Center at Hennepin County Medical Center is available 24 hours a day, seven days a week, to provide emergency information to physicians and laymen confronted with poisoning situations. Physicians should not hesitate to utilize the service and patients should be made aware of its availability. The telephone number is 612-347-3141.

Anthony S. Manoguerra, Pharm. D.*
Minneapolis, Minnesota

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*Poison Control Officer, Department of Emergency Medicine, Hennepin County Medical Center.

References

1. Barer J, Hill LL, Hill RM and Martinez WM: Fatal poisoning from salt used as an emetic. Amer J Dis Child 125:889 (June) 1973.
2. Ward DJ: Fatal hypernatremia after a saline emetic. Brit Med J 2:432 (August) 1963.
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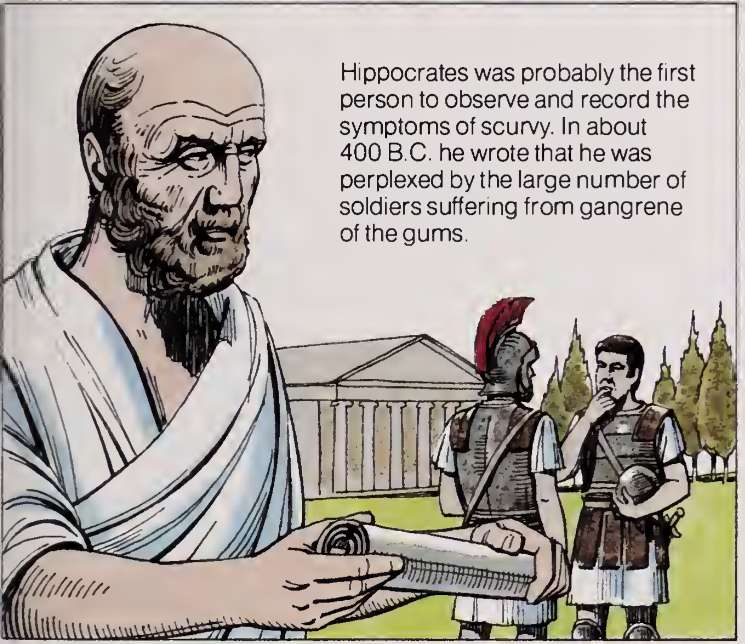
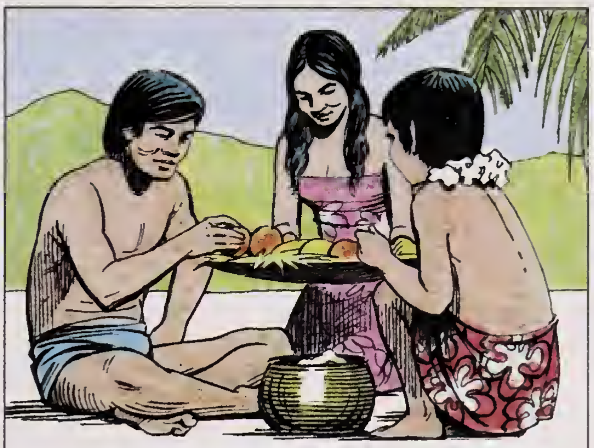


Hippocrates was probably the first person to observe and record the symptoms of scurvy. In about 400 B.C. he wrote that he was perplexed by the large number of soldiers suffering from gangrene of the gums.



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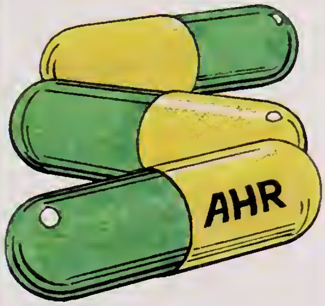

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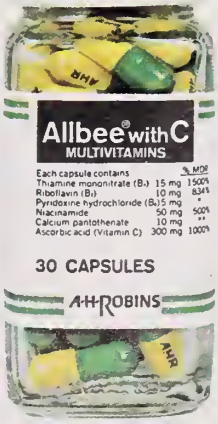

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INTERNISTS CERTIFIED or Board Eligible, for five doctor general internal medicine department in multi-specialty clinic. Subspecialty practice possible. Fine N.E. Wisconsin city of 100,000. Excellent facilities. Starting salary and fringe benefits over $46,000. Early partnership. Availability immediate thru July, 1977. Write Minnesota Medicine-513, 101 E. 5th St., St. Paul 55101.

GENERALISTS and SPECIALISTS working together to make Hartford a better place to live and practice medicine. Thirteen physicians presently serve the area in two clinics and solo practice. There is a need for more physicians to serve this fast growing area—particularly in Family Practice and Internal Medicine.

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This invitation to Hartford, Wisconsin is the Cooperative effort of the physicians, clinics, hospital and interested community leaders. Please contact: Hartford Physicians Search Committee, % N. K. Reynolds, Hartford Memorial Hospital, 1032 E. Sumner St., Hartford, Wisconsin 53027. Phone: 414-673-2300.

GENERAL PRACTITIONER to join MD in new Clinic in community of 2200; 25 miles southwest of Minneapolis; excellent schools and churches; productive farming area; 10-minute drive to hospital. Declared area of need with grant forgiveness benefits. Write or call Paul A. Stahler, M.D., Amo Vitae Clinic, 310 Sunset Drive, Jordan, Mn. 55352. 612-492-6323.

FAMILY PRACTICE positions with Mankato Clinic, Ltd., a multi-specialty group. May choose from either a satellite location in several nearby communities or, in separate department facilities in main Clinic community. Innovative and creative blending of primary and referral care in same group. Good starting salary in initial year with incentive pay thereafter; generous fringe benefits and time off allowance. For more information call collect, 507-387-1811, Wm. D. Manahan, M.D. or D. R. Molesworth, Administrator, Mankato Clinic, Ltd., Mankato, Mn. 56001.

FAMILY PRACTICE PHYSICIAN or internist wanted to join three family practitioners and one surgeon. Mpls. suburb. Crystal Medical Clinic, 5636 W. Broadway, Minneapolis, Minn. 55428. Phone: (612) 537-8413.

LOCUM TENENS/GENERAL SURGEON needed for May, June, July and August or any major part thereof for 15 doctor multi-specialty group in southern Minnesota on the scenic Mississippi River. For additional information, please write or call Dr. A. E. Edin, Chairman Recruiting Committee, Winona Clinic, Ltd., 420 E. Sarnia St., Winona, MN 55987. (507) 454-3680.

FAMILY PRACTITIONER needed to join other GP at the Pine City Clinic. New Clinic facilities including lab and x-ray. Excellent opportunity for rapid growth. Contact Oskar P. Friedlieb, M.D., 307 First Street North, Virginia, Minnesota 55792 or Ruel Martinson, M.D., Pine City Clinic, Pine City, Minnesota 55063.

CARDIOLOGY and NEUROLOGY specialty positions available with Mankato Clinic, Ltd. This multi-specialty group attracts specialty referrals from a Southern Minnesota Area of 250,000 population. Excellent group practice opportunity in medium sized community with full hospital services; full range of group fringe benefits; liberal time off; salary first year, incentive pay thereafter. For more information call collect 507-387-1811; Byron C. McGregor, M.D., or D. R. Molesworth, Administrator, Mankato Clinic, Ltd., Mankato, Mn. 56001.

WANTED—Family practitioner, board eligible or board certified, to join 10-man multiple-specialty group with emphasis on family practice. Group now consists of seven family practitioners, one surgeon, one internist and two associates in OB-GYN. Located 30 miles west of Minneapolis, in brand new clinic facilities fully equipped for 12-man group next to 105-bed, fully accredited by JACH, designated area hospital. Contact J. W. Clarke, M.D. 448-2323.

(Continued on Page 354)

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Minnesota State Medical Association

Annual Meeting

And, the winner is . . .

At the wind up festivities of last year's Annual Meeting, I overheard some say, "The people who plan the Annual Meeting, should get an award."

I will admit that securing the most qualified scientific program participants is not easy, and some complicated logistics are required to provide attendees with optimum learning facilities. Putting the Annual Meeting together needs the dedication of the Scientific Assembly Subcommittee, the State Office staff, the presidents of numerous specialty societies, and many other medical and non-medical organizations. And, without sounding like an Oscar winner's acceptance speech, I must say that much of the success of CME '76 is due to the scores of behind-the sceners who contribute significantly to the Meeting's planning. But, no one expects an award for the job he does.

Some call the job of producing the Annual Meeting an arduous task. Assembling all the parts which produce a quality convention takes much time and a generous amount of work. Numerous obstacles can impede the course of production, but we're not complaining. Every idea, every decision, every minute detail is attended to with pride and precision because you, the MSMA member, are worthy of every effort. It is you who makes us proud to be part of the Meeting.

We hope you will join us on May 20-21 at CME '76 and take part in its business and scientific sessions as well as its many social activities. Glimpses of seminar content follow. But to see what awaits you at the President's Reception and Annual Banquet, special luncheons, House of Delegates, and Friday afternoon's "Jazz Seminar," you'll have to come to Rochester. We promise you won't be disappointed. You see, we think MSMA members deserve the best . . . something special. So, each year we present the Association's most unique award, ANNUAL MEETING. And, the winner is you!

Let us honor you with CME '76.

R. D. Semsch, M.D.
Chairman
Scientific Assembly

Head and Neck Emergencies sponsored by Minnesota Academy of O & O

An informal panel discussion including such topics as nosebleeds, airway obstruction and tracheotomy, facial trauma, nasal fracture, acute laryngeal trauma, foreign bodies in nose, ears & throat and earache. Time allowed for audience participation.

Sports Medicine sponsored by MSMA Committee on Medical Aspects of Sports

Panel discussion, demonstrations, audience participation on preseason conditioning and other factors in prevention of injuries in football; on field exam and emergency procedures; weight control in wrestling; reconditioning following injuries; head and neck injuries; mouth and face injuries; facial injuries in hockey; drugs in athletics.

Emergency Laboratory Procedures sponsored by Minnesota Society of Clinical Pathologists

Communication with other specialties established need for the following five topics to be presented, after which there will be audience participation with the entire panel: 1) transfusion therapy in medical and surgical emergencies; 2) emergency blood gases (their significance and how to order); 3) blood coagulation emergencies; 4) laboratory tests in coma; 5) emergency toxicologic tests.

The Emergency Room sponsored by MSMA Subcommittee on Scientific Assembly

Stabilization of the massively injured and critically injured patient during the first hour. An audio-visual presentation with panel discussion and audience participation using actual cases from Hennepin County Medical Center Emergency and Stabilization Room.

Surgical and Medical Emergencies in Obstetrics and Gynecology sponsored by Minnesota Obstetrical and Gynecological Society

A presentation in three main categories: 1) obstetrical and gynecological surgical emergencies-diagnosis of surgical emergencies including discussion of new diagnostic techniques and review of the management of each; 2) shock in obstetrics and gynecology; management of acute bleeding; 3) management of acute toxemia of pregnancy. Question and answer periods included.

Psychiatric Emergencies—Birth to Death sponsored by MSMA Committee on Mental Health

A rational approach to the salient psychiatric emergencies seen in the age groups of childhood, adolescence, adults, and the geriatric population. Specific approaches and therapies for the problems confronting the practitioner in an emergency setting will be presented. Focus of the entire session will be on clarification of psychiatric states that often require rapid recognition, intervention and disposition. Time will be allotted for introducing audience questions.

Medical Emergencies in Adults sponsored by Minnesota Society of Internal Medicine

A formal presentation and open discussion on each of six topics: (1) transient ischemic attacks; (2) diabetic acidosis; (3) adult respiratory distress syndrome; (4) shock in acute myocardial infarction; (5) acute consumption coagulopathy; (6) tetanus. Diagnosis and emergency treatment of each disorder will be covered with particular attention to recent advances in treatment, some of which are controversial.

Medical and Surgical Emergencies of the Newborn sponsored by Minnesota Chapter, American Academy of Pediatrics

Presentations and discussion on medical emergencies with emphasis on (1) resuscitating the depressed newborn; (2) respiratory distress syndrome, especially precipitating factors and when to transport the infant; (3) emergencies in infants of diabetic mothers.

Surgical problems will include: (1) pneumothorax; (2) diaphragmatic hernia; (3) tracheoesophageal fistulas and (4) vomiting infant including problems of malrotation and volvulus, meconium ileus, duodenal atresia and other causes. Additional emergencies discussed as time permits.

Alcohol and Chemical Dependency Problems—Urgent and Emergent sponsored by MSMA Subcommittee on Alcoholism and Other Chemical Dependencies

Designed to help the practicing physician handle urgent and emergent problems arising in office and hospital practice. Major emphasis on the alcoholic with reference to other legal and illegal drugs. Topics covered to include acute detoxification, special fluid and electrolyte problems, liver failure, trauma, confrontation, commitment techniques and toxicology.

Chirurgical Emergencies (note special time for afternoon session: 2-5:30 p.m.) sponsored by Minnesota Chapter, American College of Surgeons

Presentation of papers followed by panel discussion on topics in general surgery to include: (1) ruptured abdominal aneurysms; (2) post-traumatic adult respiratory distress syndrome; (3) acute gastrointestinal bleeding and (4) ruptured sigmoid diverticulitis. Topics in specialty surgery will include: (1) acute epiglottiditis; (2) urologic emergencies; (3) surgical emergencies involving the eye and (4) neurosurgical emergencies.

National Health Planning and Resources Act: P.L. 93-641 (one session only) sponsored by Minnesota Component Society, American Society of Internal Medicine

A panel will discuss the implications of the law, especially as it relates to planning for chirurgical and medical emergencies. The views of the Federal Government and the private practitioner will be represented with ample opportunity for audience participation.

Basic Cardiac Life Support Certification (all day session) sponsored by Minnesota Heart Association

The course will begin with a plenary session reviewing the updated *Standards of Cardiopulmonary Resuscitation (CPR) and Emergency Cardiac Care (ECC)* in Basic and Advanced Cardiac Life Support. Didactic presentations in Advanced Cardiac Life Support will briefly discuss life-threatening dysrhythmias, defibrillation, and essential drug therapy in emergency cardiac care.

A Basic Cardiac Life Support (BCLS) Rescuer Course will follow. BCLS includes the following four areas: unwitnessed cardiac arrest, witnessed cardiac arrest, opening an obstructed airway, infant resuscitation. Initial Basic Rescuer certification is based on a passing grade on the cognitive test and perfection in the performance examination for an unwitnessed cardiac arrest in an adult. If time permits, participants may also take the performance examinations for witnessed cardiac arrest, opening an obstructed airway and infant resuscitation. Participants will have an opportunity for manikin practice prior to the actual certification performance. Maximum registration: 40 participants.

Since certification is based on both a passing grade on the cognitive test and a perfect score on the performance examination, registrants for this course should recognize that preparation will be necessary prior to the actual session on May 21. A packet of information will be mailed to course registrants 30 days in advance.

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e.g. the pain of
surgical convalescence

NOT TOO LITTLE
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codeine phosphate* (32.4 mg) gr ½
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SYNTHROID® (Sodium Levothyroxine, U.S.P.) Flint is not erived from any animal gland source. It is a pure synthetic. Every atch of SYNTHROID (Sodium Levothyroxine) is of controlled otency. And, it provides your patients with everything they need or complete thyroid replacement therapy.

T4, T3, or both? SYNTHROID (Sodium Levothyroxine, .S.P.) Flint is T4 which is coverted to T3 at the cellular level, proiding a physiologic source and optimal amount of T3 to meet metaolic needs for your hypothyroid patients. Because of the slower and teadier onset of action, the possibility of sudden metabolic surges is educed with SYNTHROID therapy.

SYNTHROID medication is practical and economical for longerm therapy. A recent study of 44 hypothyroid patients indicates hat 89 percent were maintained with doses of T4 (SYNTHROID) etween 100 mcg. and 200 mcg. (0.1 mg. and 0.2 mg.) per day.[1]

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Levothyroxine,
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See reverse side for full prescribing information

[1] Stock, J. M., Surks, M. I., and Oppenheimer, J. H. Replacement dosage of L-thyroxine in hypothyroidism. A re-evaluation. New Engl. J. Med. 290:529-33, 1974.

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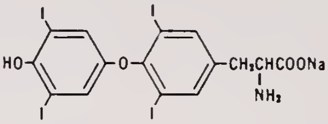
Synthroid Tablets—for oral administration
Synthroid for Injection—for parenteral administration

Description: SYNTHROID (sodium levothyroxine) **Tablets** and SYNTHROID **Injection** contain synthetic crystalline sodium levothyroxine (L-thyroxine). L-thyroxine is the principal hormone secreted by the normal thyroid gland.



Sodium Levothyroxine

Actions: SYNTHROID (sodium levothyroxine) **Tablets,** taken orally, provide hormone that is readily absorbed from the gastrointestinal tract. SYNTHROID **Injection** is effective by any parenteral route. Following absorption, the synthetic L-thyroxine provided by SYNTHROID products cannot be distinguished from L-thyroxine that is endogenously secreted. Each is bound to the same serum proteins and each exhibits a six to seven day circulating half-life in the euthyroid individual.

Both SYNTHROID products will provide L-thyroxine as a substrate for physiologic deiodination to L-triiodothyronine. Therefore, patients taking SYNTHROID products will demonstrate normal blood levels of L-triiodothyronine even when the thyroid gland has been surgically removed or destroyed by radioiodine. Administration of levothyroxine alone will result in complete physiologic thyroid replacement.

Indications: SYNTHROID (sodium levothyroxine) products serve as specific replacement therapy for reduced or absent thyroid function of any etiology. SYNTHROID **Injection** can be used intravenously whenever a rapid onset of effect is critical, and either intravenously or intramuscularly in hypothyroid patients whenever the oral route is precluded for long periods of time.

Contraindications: There are no absolute contraindications to SYNTHROID (sodium levothyroxine) therapy. Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis. (See WARNINGS)

Warnings: Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated. Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met. Clinical judgment will then dictate either a less-than-complete restoration of thyroid status or reduction in thyroid dosage.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. SYNTHROID (sodium levothyroxine) therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders.

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

Precautions: Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule. With SYNTHROID (sodium levothyroxine) **Tablets,** the relatively slow onset of action minimizes the risk of overdose but close observation in the weeks following institution of a dosage regimen is advised. Treatment of thyroid hyperactivity induced by oral medication is confined to interruption of therapy for a week, followed by reinstitution of daily therapy at an appropriately reduced dosage.

Adverse reactions: Adverse reactions are due to overdose and are those of induced hyperthyroidism.

Dosage and administration: For most adults, a final dosage of 100 mcg (0.1 mg) to 200 mcg (0.2 mg) of SYNTHROID (sodium levothyroxine) **Tablets** daily will restore normal thyroid function and only occasionally will patients require larger doses. Failure to respond adequately to a daily oral intake of 400 mcg (0.4 mg) or more is rare and should prompt reconsideration of the diagnosis of hypothyroidism, special investigation of the patient in terms of malabsorption of L-thyroxine from the gastrointestinal tract or poor adherence to therapy.

The concomitant appearance of other diseases, especially cardiovascular diseases, usually dictates a replacement regimen with initial doses smaller than 100 mcg/day (0.1 mg).

In otherwise healthy adults with relatively recent onse of hypothyroidism, full replacement dose of 150 mcg (0.15 mg) or 200 mcg (0.2 mg) has been instituted immediately without untoward effect and with good therapeutic response. General experience, however, favors a more cautious approach in view of the possible presence of subclinical disorders of the cardiovascular system or endocrinopathies.

The age and general physical condition of the patient as well as the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. In the elderly patient with long standing disease, evidence of myxedematou infiltration and symptomatic, functional or electrocardiographic evidence of cardiovascular dysfunction, the starting dose may be as little as 25 mcg (0.025 mg) per day. Further incremental increases of 25 mcg (0.025 mg) per day may be instituted at thre to four week intervals depending on patient response. Conversely, otherwise healthy adults may be started at higher daily dosage and raised to the full replacement dosage in two to three weeks. Clearly it is the physician's judgment of the severity of the disease and close observation of patient response which determines the rate of dosage titration.

Laboratory tests to monitor thyroid replacement therapy are of limited value. Although measurement of normal blood levels of thyroxine in patients on replacement regimens frequently coincides with th clinical impression of normal thyroid status, higher than normal levels on oral replacement of levothyroxine occasionally occur and should not be considered evidence of overdosage per se.

In all cases, clinical impression of the well-being of the patient takes precedence over laboratory determination in determining the appropriate individual dosage.

In infants and children, there is a great urgency to achieve full thyroid replacement because of the critica importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body size the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult, as much as 300 mcg (0.3 mg) to 400 mcg (0.4 mg) per day.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of SYNTHROID **Injection** may be administered intravenously as a solution containing 100 mcg/ml. Although the patient may show evidence of increased responsivity within six to eight hours, full therapeutic effect may not be evident until the following day. An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvement has not occurred. Like the oral dosage form, SYNTHROID **Injection** produces a predictable increase in the circulating level of hormone with a long half-time. This usually precludes the need for multiple injections but continued daily administration of lesser amounts intravenously should be maintained until the patient i fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine intravenously is clearly not without its cardiovascular risks. Under such circumstances, intravenous therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgment in this situation may dictate smaller intravenous doses of levothyroxine.

SYNTHROID **Injection** by intravenous or intramuscula routes can be substituted for the oral dosage form when ingestion of SYNTHROID **Tablets** is precluded for long periods of time.

How Supplied: SYNTHROID (sodium levothyroxine) **Tablets** are supplied as scored, color-coded compresse tablets in 6 concentrations: 25 mcg (0.025 mg)—orange . . . 50 mcg (0.05 mg)—white . . . 100 mcg (0.1 mg)—yellow . . . 150 mcg (0.15 mg)—blue . . . 200 mcg (0.2 mg)—pink . . . 300 mcg (0.3 mg)—green.

SYNTHROID (sodium levothyroxine) for **Injection** is supplied in 10 ml vials containing 500 mcg of lyophilized active ingredient and 10 mg of Mannitol, U.S.P. A separate 5 ml vial containing Sodium Chloride Injection, U.S.P is provided as a diluent.

Directions for reconstitution: Reconstitute the lyophilized sodium levothyroxine by aseptically adding 5 ml of the Sodium Chloride Injection, U.S.P to the vial. Shake vial to insure complete mixing. **Use Immediately** after reconstitution. Discard any unused portion.

U.S. Pat. 2,889,363

January 1975

Special Article

Long Term Anticoagulant Therapy following Myocardial Infarction

DOUGLAS H. JOHNSON*

A group of 135 men and women who sustained their first myocardial infarction were given long term anticoagulant therapy. The effect of the anticoagulant on preventing death due to recurrent myocardial infarction was determined by comparisons with control groups taken from the literature. A statistically significant decrease in death rate due to recurrent myocardial infarction for up to ten years was found in patients maintained on adequate long term anticoagulant therapy when compared with control groups taken from the literature.

THE EFFICACY OF LONG term anticoagulant therapy in the post-myocardial infarction patient has been controversial. This study was designed to determine the effectiveness of long term anticoagulant therapy on preventing recurrent myocardial infarction (MI) and to determine whether different levels of anticoagulation have an effect on the recurrence of MI.

Method

One hundred thirty-five consecutive patients (101 men and 34 women) who had suffered their first MI and survived longer than one month were included in the study. The patients were under the care of two internists in private practice. Diagnosis of MI was made on the basis of clinical history and physical findings supported by classic electrocardiographic changes and/or enzyme studies. All the patients received anticoagulants in the hospital and on a continual long term basis. At the time of this study patients had been treated from six months to 17 years, for a total of 738 person-years. Bishydroxycoumarin or sodium warfarin were used as anticoagulants. Patients were from all walks of life; the average age at which the MI occurred was 56 years. Prothrombin times were done by the Quick one-stage method in a commercial laboratory every two to three weeks, with the results and anticoagulant dosage schedules given the patient by telephone.

Survival curves were calculated by the actuarial method as described by Berkson and Gage.[1] Death rates or reinfarction rates were calculated as the number of such events per 100 person-years at risk.

Because of the nature of the medical practice in which the study was done, it was not feasible to have a satisfactory control group. Therefore, to determine the value of long term anticoagulation the data of control groups from four large anticoagulant studies were used.[2-5] These control groups encompassed some 6511 patients observed from one to 10 years, and were used for comparison with our anticoagulated patients. Both our anticoagulant group and the control group patients were included only after recovery from their MI; patients who died before leaving the hospital were not counted in either series. Because each of the articles expressed their control group data in different ways, i.e. average mortality rate, age categories, etc. sufficient data were not available in each article to express all of the control studies in the same format. Therefore when comparing our statistics with a control group we expressed our data in the same manner as that of the control group under comparison.

Before criticism is raised as to this manner of obtaining control groups for such a study, the

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*Student, Mayo Medical School, Rochester, Minnesota.

All of the anticoagulant patients were under the care of Herbert W. Johnson, M.D. and Kjeld O. Husebye, M.D., 715 Lowry Medical Arts Bldg., St. Paul, Minn.

Sincere thanks are due Drs. Johnson and Husebye for the assistance they provided, and to William F. Taylor, Ph.D., Dept. of Statistics, Mayo Clinic, Rochester, Minn. for help with the statistical work.

reader should be aware that cooperative methods were used to obtain control groups as well as anticoagulated patient groups in all the articles we have cited. Fifteen separate centers in one,[2] nine separate groups in another,[3] fourteen separate centers in a third,[5] and a group practice in the fourth[4] were used to obtain patients. These represented not only separate medical centers but also different countries and multiple groups of physicians.

Three of the four studies[2-4] used total mortality in their calculation of death rates. When comparing our group with these studies we also used total mortality in our calculations. These studies also estimated that deaths due to cardiovascular disease represented 80 to 85% of the total mortality.* Because we were interested specifically in cardiovascular deaths, we lowered the death rate figures for the control groups by 20% and compared them with our cardiovascular statistics. In making comparisons with papers that included congestive heart failure as a cause of cardiovascular death we also included CHF; when comparing with papers using deaths due to MI only we also used deaths due to MI only.

Results

Characteristics of Anticoagulated Group

Survival rates for our total group as well as for men and women within the group were calculated.

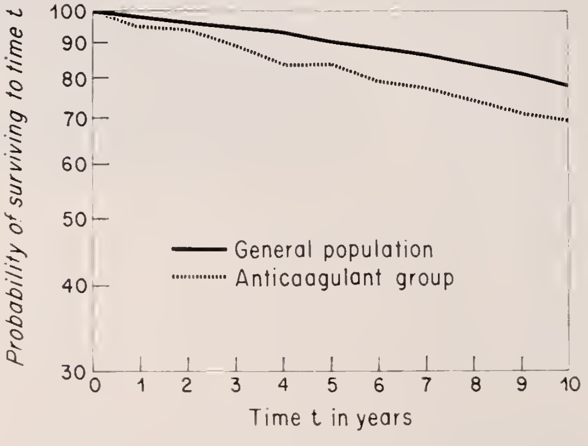

Fig. 1—Probability of surviving for the anticoagulated group vs. the expected survival curve for the general population of same age and sex distribution, considering all causes of death.

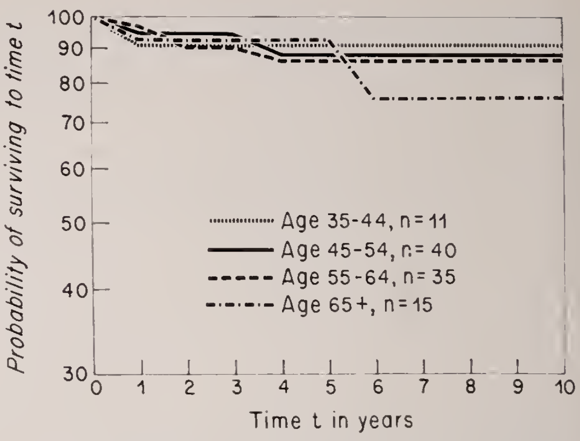

Fig. 2—Probability of remaining free from reinfarction, fatal or non-fatal, in the anticoagulated group. Time measured from first infarction.

Figure 1 shows the expected survival curve for the general population and the survival curve for our anticoagulated group. Both curves consider deaths from all causes; the general population used has the same age and sex distribution as our group. The anticoagulant group has a significantly lower overall survival rate than the general population. This is to be expected, as patients in the anticoagulated group have had one MI and are expected to be at greater risk of another infarct. Of importance, however, is the finding that there is no unusual pattern of death in the treated group, demonstrated by the similar shapes of the survival curves.

Males in the treated group had a lower reinfarction rate (both fatal and non-fatal) than females (males: 2.2 per 100 person-years, females: 5.8) and a lower mean annual death rate from reinfarction (males: 1.3, females: 3.2). These differences, however, are not statistically significant. No significant difference was found between the rates of reinfarction for men over 55 years and those under 55 years (men over 55: 2.7 per 100 person-years, men under 55: 2.2) or the mean annual death rates from reinfarction (men over 55: 1.9, men under 55: 1.2) during 17 years of treatment.

Figure 2 shows the probability of remaining free from reinfarction (both fatal and non-fatal) for men in the anticoagulant group by ages. There was no significant difference in the reinfarction-free survival rates of men ages 35-44, 45-54, 55-64, and 65 + up to 10 years. These rates were, respectively, 90.9, 87.8, 86.2, and 76.0%.

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*Data from the Coronary Drug Project Research Group study published in 1975 indicates that cardiovascular deaths account for 86 and 89% of all causes of death in patients who have had one MI and have not received long term anticoagulation.[6] This is roughly in agreement with the 80 to 85% figures mentioned above.

An evaluation of the effect of the prothrombin time level on the survival rate of the group was made. The mean prothrombin time for each patient was calculated and used to place him in one of three groups: (1.) mean prothrombin time 17.0 to 20.6 seconds, group mean 19.5 sec. (normal: 12 sec.), (2.) 20.7 to 22.0 sec., group mean 21.4 sec., (3.) 22.1 to 25.2 sec., group mean 23.0 sec. It should be noted that only six patients averaged below 18.5 sec.

No significant difference in the reinfarction rate was found between any of the three groups; no significant difference in the rate of fatal reinfarction was found which related to the level of anticoagulation used in the study.

Comparison with Control Groups of Four Major Studies

1. The Veterans Administration Study Control Group:[2] Table 1 shows comparable mean annual death rates, considering both deaths from all causes and deaths from MI. After seven years of observation (the length of the V.A. study) our treated group had a significantly lower mean annual death rate in both total mortality and deaths from reinfarction.

2. The collaborative analysis of nine different reports of anticoagulant trials reported by the International Anticoagulant Review Group in *Lancet*, 1970:[3] Table 2 shows a comparison of age-specific death rates for men. A comparison is also made for the age groups over 55 years and under 55 years, and for the group total. There is a significantly lower death rate in our anticoagulant group for all patients over 44 years when considering both total mortality and deaths due to cardiovascular causes.

TABLE 1
Death Rates per 100 Person-Years for Anticoagulant Group and V.A. Control Group.[2]

	Control Group	Anticoagulant Group
mean age	51.2	54.8
no. of men	350	101
person-years exposure	1439	446
deaths all causes	113	18
death rate	7.85	4.04*
deaths MI caused	85	8
death rate MI deaths	5.91	1.79*

MI figures for the control group are estimated by lowering the total number of deaths 20%, as estimated in the V.A. Study.
*Difference between control and anticoagulated group is statistically significant at p=0.01

3. The Suzman Study, published in 1971:[4] This 10-year study covers the longest time span we found reported in the literature. A comparison of the mean annual death rate was made for all patients (men and women, all ages) combined. A significantly smaller death rate for all causes of death and for cardiovascular disease is evident in our anticoagulant patients, as shown in Table 3.

4. The Second Report of the Working Party on Anticoagulant Therapy in Coronary Thrombosis, reported in the *British Medical Journal*:[5] A comparison of yearly death rates from MI for men over 55 years and under 55 years, and for all men after four years of observation is shown

TABLE 2
Death Rates per 100 Person-Years Exposure for Anticoagulant Group and "International Review Group" Control Group.[3]

Age	Person-Years Exposure	Deaths All Causes	Death Rate	Deaths CV Caused	Death Rate CV Deaths
Control group					
35-44	678	42	6.2	36	5.3
45-54	1069	83	7.8	70	6.6
55-64	1141	117	10.3	99	8.7
65+	647	93	14.4	79	12.2
<55	1799	129	7.2	109	6.0
≥55	1788	210	11.7	178	10.0
TOTAL	3591	340	9.4	289	8.0
Anticoagulant group					
35-44	71	1	1.4	1	1.4
45-54	265	9	3.4*	7	2.6*
55-64	190	10	5.3*	6	3.2*
65+	69	3	4.3*	3	4.3*
<55	336	10	3.0*	8	2.4*
≥55	259	13	5.0*	9	3.5*
TOTAL	595	23	3.9*	17	2.9*

CV figures for control group are estimated by lowering the total number of deaths 20%, as estimated in the "International Review Group" Study.
*Differences between control and anticoagulant group are statistically significant at $p<0.01$

on Table 4. Our treated group had a significantly lower death rate for men over 55 years after three years, and for men under 55 years after four years of observation.

Discussion

Our study shows that death rates among 135 patients treated with anticoagulants over a 10-year period were considerably (and statistically significantly) less than rates for four different control groups of MI patients not on long term anticoagulant therapy. The benefits derived were not age or sex dependent. Frequent visits to the physician did not play a part in the results, since they averaged only four times per year; all anticoagulant dosage schedules were transmitted to the patients by telephone through the office help.

Anticoagulant therapy is not without complications. The patient's and physician's time involved in maintaining adequate therapy, the expense to the patient and the potential hazards of hemorrhage must be considered before a patient is placed on long term anticoagulant therapy. Seven of our patients had significant gastrointestinal bleeding (five of these patients remain anticoagulated); four patients had hematuria (all remain on anticoagulants); two had rectal bleeding —one of which was secondary to carcinoma of the colon (both remain anticoagulated); and one patient died of intracranial hemorrhage after a fall.

TABLE 3

Death Rates per 100 Person-Years for Anticoagulant Group and Suzman Control Group.[4]

	Control Group	Anticoagulant Group
mean age	58.5	56.4
no. of people	992	135
person-years exposure	4323	663
deaths all causes	459	31
death rate	10.6	4.7*
deaths CV caused	391	24
death rate CV deaths	9.0	3.6*

CV figures for control group are estimated by lowering the total number of deaths 20%, as estimated in the Suzman Study.

*Differences between control group and anticoagulant group are statistically significant at $p = 0.01$.

Interestingly, of the 14 patients who stopped anticoagulant therapy, four died of myocardial infarction (and a fifth had a non-fatal MI) within six months, one died of cerebrovascular thrombosis within two months, and one died of a mesenteric thrombosis four months after discontinuing anticoagulation. This same type of increased fatality rate and increased MI rate was noted in the V.A. study.[7] They stated that within seven months of stopping anticoagulants there were eight deaths while the control group had only two; within the same seven month period after stopping anticoagulants there were seven non-fatal myocardial infarctions while the control group suffered only two.

Conclusions

1. A statistically significant decrease in the death rate from all causes of death and from recurrent myocardial infarction was found after 10 years of observation in patients who had sustained a myocardial infarction and were maintained on adequate long term anticoagulant therapy, when compared with post-myocardial infarction non-anticoagulated control groups taken from the literature.

TABLE 4

Death Rates per 100 Person-Years Exposure for Anticoagulant Group and "Working Party" Control Group.[5]

	Control Group			Anticoagulant Group		
Men <55	Person-Years Exposure	Deaths MI Caused	Death Rate	Person-Years Exposure	Deaths MI Caused	Death Rate
1 year post-MI	101.3	15	14.8	49.0	2	4.1*
2 "	20.8	3	14.4	42.5	0	0.0*
3 "	5.3	0	0.0	39.0	0	0.0
4 "	0.1	0	0.0	35.0	1	2.9
cumulative (after 4 yrs.)	127.5	18	14.1	165.5	3	1.8*
Men ⩾55						
1 year post-MI	145.7	16	11.0	47.0	2	4.3
2 "	39.3	1	2.5	40.5	2	4.9
3 "	7.9	0	0.0	34.5	0	0.0
cumulative (after 3 yrs.)	192.9	17	8.8	122.0	4	3.3*
All Men cumulative (after 4 yrs.)	320.4	35	10.9	287.5	7	2.4*

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*Differences between control group and anticoagulant group are statistically significant at $p = 0.01$.

2. Anticoagulated patients had a significantly lower age-specific death rate from all causes of death and from recurrent myocardial infarction in the age groups 45-54 years, 55-64 years, 65+ years than did the post-myocardial infarction non-anticoagulated control group collected from the literature.

3. No significant difference in reinfarction rate was found between men and women on anticoagulant therapy.

4. No significant difference in the reinfarction rate was found between anticoagulated patients in the age groups 35-44 years, 45-54 years, 55-64 years, 65+ years.

5. Provided the prothrombin time was kept within the therapeutic range, (19.5 to 23.0 sec., normal = 12 sec.) no significant difference in death rate from recurrent myocardial infarction was found to be dependent on the level of anticoagulation.

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Cover Photo
“Mayo Building-Mayo Clinic”

Dr. Don A. Scholz, a physician in endocrinology and internal medicine at the Mayo Clinic for 17 years, took the cover photo from the garden extrance of the Mayo Medical Museum. It shows the north entrance into the Mayo Clinic-Mayo Building. He used a Nibon F camera.

His photographs have won a variety of awards for superior photography, including the Newspaper National Snapshot Award in 1963, and the Internal Medicine News Monthly Award in 1974. One of his photographs was published on the November, 1969, cover of MINNESOTA MEDICINE.

American Board of Family Practice

The American Board of Family Practice announces the next certification examination will be given October 30-31, 1976. The two day written examination will be held in seven cities geographically distributed throughout the United States. Information regarding the examination may be obtained by writing:

Nicholas J. Pisacano, M.D., Executive Director & Secretary
AMERICAN BOARD OF FAMILY PRACTICE, INC.
University of Kentucky Medical Center
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Please note: It is necessary for each physician desiring to take the examination to file a completed application with the Board office. Deadline for receipt of applications in this office is June 15, 1976.

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Few would disagree that the effectiveness and safety of any therapeutic agent or device must be determined through clinical research.

But now the *practice* of clinical research is under appraisal by Congress, the press and the general public. Who shall administer it? On whom are the products to be tested? Under what circumstances? And how shall results be evaluated and utilized?

The Pharmaceutical Manufacturers Association represents firms that are significantly engaged in the discovery and development of new medicines, medical devices and diagnostic products. Clinical research is essential to their efforts. Consequently, PMA formulated positions which it submitted on July 11, 1975, to the Subcommittee on Health of the Senate Labor and Public Welfare Committee, as its official policy recommendations. Here are the essentials of PMA's current thinking in this vital area.

1. PMA supports the mandate and mission of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and offers to establish a special committee composed of experts of appropriate disciplines familiar with the industry's research methodology to volunteer its service to the Commission.

2. PMA supports the formation of an independent, expert, broadly based and representative panel to assess the current state of drug innovation and the impact upon it of existing laws, regulations and procedures.

3. When FDA proposes regulations, it should prepare and publish in the *Federal Register* a detailed statement assessing the impact of those regulations on drug and device innovation.

4. PMA proposes that an appropriately qualified medical organization be encouraged to undertake a comprehensive study of the optimum roles and responsibilities of the sponsor and physician when company-sponsored clinical research is performed by independent clinical investigators.

5. PMA recognizes that the physician-investigator has, and should have, the ultimate responsibility for deciding the substance and form of the informed consent to be obtained. However, PMA recommends that the sponsor of the experiment aid the investigator in discharging this important responsibility by providing (1) a document detailing the investigator's responsibilities under FDA regulations with regard to patient consent, and (2) a written description of the relevant facts about the investigational item to be studied, in comprehensible lay language.

6. In the case of children, the sponsor must require that informed consent be obtained from a legally appropriate representative of the participant. Voluntary consent of an older child, who may be capable of understanding, in addition to that of a parent, guardian or other legally responsible person, is advisable. Safety of the drug or device shall have been assessed in adult populations prior to use in children.

7. PMA endorses the general principle that, in the case of the mentally infirm, consent should be sought from both an understanding subject and from a parent or guardian, or in their absence, another legally responsible person.

8. Pharmaceutical manufacturers sponsoring investigations in prisons must take all reasonable care to assure that the facilities and personnel used in the conduct of the investigations are suitable for the protection of participants, and for the avoidance of coercion, with a respect for basic humanitarian principles.

9. Sponsors intending to conduct nontherapeutic clinical trials through the participation of employee volunteers should expand the membership and scope of its existing Medical Research Committee, or establish such an internal Medical Research Committee, with responsibility to approve the consent forms of all volunteers, designs, protocols and the scope of the trial. The Committee should also bear responsibility to ensure full compliance with all procedures intended to protect employee volunteers' rights.

10. Where the sponsor obtains medical information or data on individuals, it shall be accorded the same confidential status as provided in codes of ethics governing health care professionals.

11. PMA and its member firms accept responsibility to aid and encourage appropriate follow-up of human subjects who have received investigational products that cause latent toxicity in animals or, during their use in clinical investigation, are found to cause unexpected and serious adverse effects.

12. PMA supports the exploration and development by its member companies of more systematic surveillance procedures for newly marketed products.

13. When a pharmaceutical manufacturer concludes, on the basis of early clinical trials of a basic new agent, that a new drug application is likely to be submitted, a proposed development plan accompanied by a summary of existing data, would be submitted to the FDA. Following a review of this submission, the FDA, and its Advisory Committee where appropriate, would meet with the sponsor to discuss the development plan. No *formal* FDA approval should be required at this stage. Rather, the emphasis should be on identification of potential problems and questions for the sponsor's further study and resolution as the program develops.

The PMA believes that health professionals as well as the public at large should be made aware of these 13 points in its Policy on Clinical Research. For these recommendations envisage constructive, cooperative action by industry, research institutions, the health professions and government to encourage creative and workable responses to issues involved in the clinical investigation of new products.

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Twenty-Five Years of Amalgamation of Psychiatry with Obstetrics—Gynecology at the University of Minnesota

IRVING C. BERNSTEIN, M.D.,* JOHN M. McKELVEY, M.D.,† and
JOHN J. SCIARRA, M.D.‡

The history of 25 years association of a psychiatrist with a medical school Department of Obstetrics and Gynecology is described including its problems, development and progress. The medical model is emphasized and psychiatry is demonstrated as similar to general medicine in having pathology demonstrated, treatment effected, and dispositions made. The recommendation is made that a Medical School Ob Gyn Department can benefit greatly by having a full time psychiatrist available not only for management of psychiatrically ill patients, but for prevention, teaching and research in all the various clinics and wards of an Ob-Gyn Department.

For a quarter of a century a psychiatrist has been a member of the Department of Obstetrics and Gynecology at the University of Minnesota Medical School. In fact, today he is the senior member of the Obstetrics and Gynecology Staff in terms of time. This period has been a continuing growth experience filled with multiple challenges for the psychiatrist. The challenge started in 1951 when an application was made to the head of the Obstetrics-Gynecology Department for an opportunity to join his staff and teach the psychiatric aspects of obstetrics and gynecology to his students and residents. He was mildly interested and after much interrogation on his part as to what was intended, he offered a contract which was adhered to until his retirement. "I will give you a position in this department if it is agreed that you can be discharged at any time, but can never quit." The psychiatrist was so eager to be a member, even with no salary, that this strange contract was agreed to without his realizing the implications.

Doubts

It was obvious in many more subtle ways that the Obstetrics-Gynecology Department head had considerable doubts as to what a psychiatrist could do that would be of value for him, his staff, his students and his department, which included referring difficult cases and asking for quick results. The psychiatrist was prepared for this, since he had been trained under a professor who had always emphasized to his staff and residents that most doctors, and especially heads of clinical departments, have grave doubts as to the value of psychiatric assistance. Most feel a psychiatrist has little to offer in a practical sense for psychosomatic problems, except to provide a history, and maybe a strange diagnosis and some assistance in managing behavior problems. The behavior problems are referred with the request to try some psychotherapy, however defined, and a vicious cycle is apt to be established since this type of patient is usually a poor candidate for psychotherapy. Lipowski[1] wrote: "Their negative attitudes are often expressed subtly and jovially and are sometimes disguised with effusive cordiality. The enmity of a department head may thwart liaison work." To counteract these negative attitudes, the psychiatrist had been trained to always provide service. With this in mind, the program at Minnesota was directed toward service and utilizing the routine Obstetric-Gynecology patients for teaching purposes.

Acceptance

After many hours of planning, the proposed program was accepted with some reservations by the department head. Complete acceptance by

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him and his staff was a gradual process and took about two years. Since then the problem has become the plethora of referrals; thus research has been limited, although a number of papers have been published. At the beginning, a half day per week was provided—now about two half days per week at the Medical School are scheduled and a salary is budgeted.

Practical and Positive Approach

In providing psychiatric diagnostic and therapeutic service for the department, the practical aspects of psychodynamics and psychiatry are taught with special emphasis placed on the positive effects of the patient-doctor relationship. The teaching is accomplished using usual medical terminology rather than psychiatric jargon, and in a manner designed to avoid confusing or antagonizing the students and staff. For example, in discussing the emotional aspects of medications, it is emphasized that drugs are beneficial not only because of physiological effects, but also because they are evidence of the doctor's continuing concern with the patient and his illness.

Similarities to General Medicine

Psychiatry is demonstrated as similar to general medicine in having pathology demonstrated, treatment effected, and disposition made, usually by the psychiatrist alone, without the assistance of social workers and psychologists. The team approach in psychiatry, where all members of the health team are equal was never taught or utilized. Criticism was leveled by some colleagues at this approach—but not, interestingly enough, by the Ob-Gyn Staff.

Today the pendulum is swinging back to this conclusion. John Spiegel,[2] immediate past President of the American Psychiatric Association, stated in his presidential address of 1975, "The medical training of the psychiatrist enables him to provide a wider range of information during a discussion than other professionals. Because of our access to information and resources, I like to think of psychiatry as prescriptive—an information bureau serving as a gateway to services provided by other professionals. This does not mean we will have mandated controls over the other professionals. Rather, it indicates we will continue to be viewed as having more to offer to the operation of the system of care in general, and to the treatment of mental illness in particular, than the other professions."

Changing Attitude Towards Psychiatry

The essential part of the teaching program involves discussion of the problems of patients who are referred for psychiatric consultation and for management. Discussion is done cautiously because both staff and students may have been negatively conditioned in their attitudes toward psychiatry. Dennis Hill[3] states, "Medical students' attitude towards psychiatry—too often found to be either uncritical acceptance or uncompromising rejection—depends to a large extent on his childhood experiences, school and preclinical training, and is liable to reinforcement by his clinical experience and first contacts with psychiatry itself.

"The medical students in general have been exposed to insufficient or inadequate teaching of psychology and sociology in college; have been exposed to much hostility toward psychiatry by admired medical teachers with those attitudes they tend to identify; have been exposed to excessive emphasis on psychopathology and psychological determinism which might have aroused intense anxiety in them, particularly in being exposed in early experiences in psychiatry to the severely ill in-patient—the psychotic or character disorder—precisely those patients who are the most troublesome to society and in whom results are the poorest. The utilization of these severely ill patients to teach medical students to use psychiatry principles in general medicine is unwise."

Importance of Evaluating Personality

The importance of a personality evaluation in every presenting patient is emphasized. Each patient is to be regarded as a person, the product of his environment, whose reaction to illness is based on his personality and whose personality is influenced by the illness. Smyth[4] states this well. "To know what kind of person has a disease is as essential as to know what kind of a disease a person has."

The students and residents are taught that the initial history should include information about the setting of the illness and something of the patient's past and current life situation, without the patient being made to feel an irrelevant and intrusive psychiatric inquiry is being made. After the history and physical examination is completed, and the medical diagnosis is made, the workup is not considered, complete until a diagnosis of the patient's mental condition is made in a general way. At a minimum, each patient should be classified as normal, neurotic, psychotic, psychopathic, or organic.

To help the student understand the value of the mental status and what it indicates, a one hour lecture on psychopathology is given to each clerkship group. The relationship between a patient's psychopathology and the treatment of the patient's physical illness is demonstrated. The importance of early childhood experiences in determining whether one eventually becomes normal, neurotic, psychotic, or sociopathic is emphasized. Psychotherapy or the manipulation of the patient-doctor relationship in order to accelerate medical treatment is shown as being more effective the later in childhood the experiences occur.

The student is made aware that the personality of the patient can in great degree determine the effectiveness of the treatment of a disease process. This may be demonstrated vividly in the treatment of a pregnant diabetic patient who might also be neurotic, psychotic, or psychopathic. Being able to predict what happens in psychiatric patients as well as patients in general is demonstrated to be satisfying and worthwhile. Knowing that poor results will probably be attained in treatment of a diabetic pregnant psychopath, while good results can be predicted in treatment of a diabetic obsessive compulsive patient, is useful and can reduce despair and hostility in the treating physician. Medical students participating in such experiences usually develop a more positive attitude towards the value of psychiatry to general medicine.

Using Psychiatry to Alleviate Symptoms

To emphasize the value of "psychiatric knowhow," symptoms have to be eradicated or at least alleviated. Phlebotomy does not cure congestive heart failure but it may be dramatic and helpful. Similarly effective treatment of nausea and vomiting of pregnancy, urinary retention following delivery, some cases of vulvar itching, or hypochondriasis are dramatic. Urinary retention after delivery is an interesting symptom. If the physical examination is negative and the usual modalities of treatment have failed the patient is told a psychiatrist will be in to see her if she cannot urinate. With this suggestion many will micturate. Those who do not, have been treated effectively by hypnosis. Dynamically these patients may be utilizing this symptom to prolong the hospitalization and avoid the responsibility of caring for the new baby.

Dramatic disappearance of persistent vulvar pruritis has occurred after recognizing and treating the emotional components. One patient with severe scarring as a result of vulvar itching was referred prior to her scheduled vulvectomy. In three successive daily interviews she abreacted considerable traumatic material. She was certain she had a venereal disease and had been too ashamed to talk about it. She had gone from doctor to doctor because of the discomfort in this area but had never admitted her fears to them. They had treated her with many modalities including Xray, but her itching was not relieved and she continued to scratch. As a result of these interviews, including reassurance that she did not have a venereal disease, her itching lessened, and the surgery was cancelled. Because of the alleviation of her symptomatology she subsequently participated more often in intercourse and within a year conceived and delivered after years of infertility.

Giving Formal Lectures

Each medical student while on the Ob-Gyn clerkship has from five to seven one hour formal lectures. These include psychosexual development, and the treatment of the chronic complainer. In the days before Masters and Johnson the third lecture was on nausea and vomiting of pregnancy —now it is on treatment of sexual disorders. The remaining sessions vary with the material presenting on the ward and may include homosexuality in gynecological practice, nausea and vomiting of pregnancy, pruritis vulvae, marriage therapy, urinary retention, anovulatory agents, abortion, pelvic and abdominal discomfort, sterilization, infertility, dysmenorrhoea, and terminal cancer.

Discussing Hypochondriasis

Hypochondriasis is discussed in detail because it is such a common problem. By the time medical students are in the third year, the concept of "the crock" is well established. The student, as well as most of his teachers in medical school, feel frustrated, hopeless and inadequate when confronted with a patient who gives a detailed history of being miserable and not being helped by many doctors using many different modalities of treatment. In the treatment process the student is made aware of his own feelings towards such patients, and how to utilize these feelings in making the diagnosis of hypochondriasis. Steiger[5] says, "Awareness of his own subjective feelings and that they arise from the patient allows the physician to make a diagnosis quickly, whereas a strictly objective approach may lead to multiple expensive laboratory testing." The student is taught how these patients may be cared for through an understanding of the psychopathology involved and the utilization of a patient-doctor relationship together with drugs and limiting dependency in the manner described so well by Lyon.[6] In this methodology the student learns that hypochondriacal patients need their symptoms to adjust to their environment. Their symptoms are necessary "emotional crutches." It is shown that surgical attempts to remove these symptoms only make the patients worse after an initial improvement, and that they need to be treated over long periods of time with regular scheduled visits by an understanding physician who will listen to their complaints and prescribe symptomatic, non-addicting drugs. Eventually most students accept the premise that medications, considered in psychoanalytic terms, are substitutes "for the breast."[7]

Understanding Chronic Complainers

The obstetrical gynecological staff uses this technique with beneficial results not only for their patients, but for themselves. After some experience, they no longer feel hostile and uncomfortable with chronically complaining patients devoid of organic pathology. The diagnosis of hypochondriasis, like all psychiatric illnesses, must not be made by exclusion, but on the basis of a history of constant complaining, many surgeries and workups and no improvement. Ordering every possible laboratory test in such a case has some real disadvantages. Among the most serious of these is the strengthening of the patient's conviction that she is in reality suffering from an unrecognized organic disease. The extent of mechanical and chemical investigation of these patients should be limited to a safe minimum, keeping in mind the possibility that the hypochondriacal patient may also have or develop an organic illness. The fact that some hypochondriacal patients "improve" dramatically and complain less when they develop a severe physical illness is explained. These patients now have an illness which their family and friends can accept and which can be used as an excuse for their inability to adjust, so they do not have to complain as much any more.

Handling Hypochondriasis by Knowing the "Little Things"

While studying hypochondriasis the student is shown how important the "little things" are. The importance of limiting the length of interviews, the importance of not answering the telephone during office visits except for emergencies, and the importance of being on time are stressed. If the length of interviews is not scheduled, the patient has a tendency to continue to talk on and on. If the patient knows exactly when she is to return, she will leave readily at the end of her scheduled time. The patient will realize her doctor is giving her his undivided attention if he does not answer the telephone except for emergencies. She also learns that she cannot talk to him without an appointment unless an emergency exists. She is thus discouraged from calling him unnecessarily. If the doctor tends to be on time, the patient will be on time and not be hostile with the doctor. In caring for the "little things" the doctor is enhancing and manipulating the doctor-patient relationship positively, which is extremely important in treating all patients and avoiding malpractice suits. The understanding or the symptom complex of hypochondriasis, more than anything else taught in the Ob-Gyn clerkship, has helped more students to accept psychiatry as a useful tool.

Managing Nausea and Vomiting

Severe nausea and vomiting[8] once was a frequent complaint in patients in an obstetrical department. It is now less common but the occasional case still presents. Nothing is more dramatic and useful in demonstrating the effectiveness of the patient-doctor relationship than to alleviate this symptom with an interview or two. This has been done on many occasions although some of the more severe cases do not respond as quickly. Students observing a psychiatrist being involved in the treatment of these severely ill and dehydrated patients tend to develop a more positive feeling about psychiatrists. The psychiatrist is then in an ideal position to demonstrate how severe psychopathology can threaten a patient's life by other means than suicide.

Looking Back

In the past quarter century at Minnesota there have been only two department heads of the Ob Gyn Department, except for interim short period temporary heads who have also been most tolerant of psychiatry. The latter have essentially carried out the plans of their predecessors. The second head's appointment was coincident with the change in the medical school curriculum, which among other things, de-emphasized psychiatry.[9] Because of the change there was less time available in the Ob Gyn clerkship for teaching psychiatric aspects of Ob Gyn.[10] But as time passed, the new head reinstated the teaching program, and in addition delegated more responsibility. He felt that the Clinical Staff should be better organized and more appropriately recognized. The psychiatrist was appointed to chair the clinical faculty committee. The appointment of a psychiatrist to this position did not please all of the clinical staff, but as time progressed, most of the dissidents seemed satisfied with the accomplishments of the committee. Their duties included appropriate promotions, occasional threats of termination of appointments, the organization of two social events per year, which are well attended. One is for staff alone, and here complaints are aired. One is purely social and is for staff and spouse/guest. These events helped to bridge the gap between "town and gown."

Value of Travel and Meeting

The new department head encouraged more travel and participation in international and national meetings. This has produced a wider understanding of what has been accomplished psychiatrically in the Minnesota Ob Gyn Department. It has brought back to Minnesota what is being done elsewhere. One example of this was the opportunity to spend a week at the Institute of Reproductive Biology with Masters and Johnson. This resulted in bringing their techniques and insights to the staff and students of the Ob Gyn Department, and also to other physicians in Minnesota through presentations at grand rounds and at staff meetings of other local hospitals.

Looking Ahead

In retrospect the past 25 years have been eventful, challenging, and a growth experience. It could have been even better if more time had been available. It is clear now that the department of Ob Gyn should have a full time psychiatrist who has the complete backing of the department head. The acceptance of the psychiatrist by the head of the service is an essential requirement if the program is to succeed. This psychiatrist should be intimately involved, not only with the management of ill patients, but should be available for prevention, teaching, and research in the Gynecology Clinic, in the Infertility Clinic, in the Endocrine Clinic, in a Sex Clinic, and of course in the Obstetrics Clinic. Where else could a psychiatrist be more valuable in prevention of psychiatric illness than being a consultant and educator of the doctors in an Ob Clinic with its potential of new mothers. Here the obstetrician has the opportunity to treat a young, usually motivated patient periodically, who feels he is not only her doctor, but her teacher, counselor, confidant, and psychiatrist. The obstetrician with his limited training in psychotherapeutic techniques may not be able to change his patient basically, but he should be encouraged to help his patient raise her child more effectively. He should emphasize the importance of providing the newborn child with love, security, and acceptance and avoiding subjecting the child to fear, isolation, unnecessary pain, and anxiety. He should also impress upon the mother the significance of raising the girl as a girl and the boy as a boy, and to inculcate in them healthy attitudes on anatomy, physiology, and sex. If this is done, they will be better equipped to handle all future problems, including pregnancy and marriage.

Besides the obvious involvement with clinical aspects of the Ob Gyn Department, the departmental psychiatrist's expertise could be helpful in evaluating potential residents and staff.

Resume

A short resume has been presented of the involvement of a psychiatrist with a department of Ob Gyn at Minnesota, what he is presently doing, and what it is hoped the program will become. Having a psychiatrist intimately involved with an Ob Gyn Department can be of real value to both the department and its patients. This amalgamation is recommended. The psychiatrist chosen for such a position should be one who is interested in teaching and who enjoys identifying with the general practice of medicine. He should be adept in administration, and eager to do collaborative research. He must be able to handle appropriately both the negative and positive feelings about psychiatry which may present in the obstetrical gynecological staff and in the students.

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Acute Phase of Myocardial Infarction—Adgey et al. (page 353)

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Quinton Exercise Testing Seminar
Rochester Methodist Hospital
May 19—Rochester

7:30—Registration, Materials Distribution

8:15—Rationale of Exercise Tests: Magnitude of the heart disease problem; Exercise and heart disease; Physiology of exercise; Myocardial oxygen demand.

9:00—Indications and Contraindications

9:45—Types of tests, equipment: Maximal; Sub-maximal; Balke; Bicycle; Bruce; Ellestad; Naughton; Stop; Treadmill; Costs; Methods; Advantages; Disadvantages.

10:45—Performance of the Test: Pretest screening; Consent form; Personnel; Electrodes; ECG Monitoring; Performance of the test; Indications of stopping test; Safety, risk, litigation.

11:45—Results of Exercise Testing: Pulse response; Blood pressure; Observation of patient; Exercise capacity; Electrocardiographic results.

1:45—Demonstration: A complete clinical live stress test demonstration from patient screening through post test observation.

3:15—Interpretation: ECG Analysis of exercise test; Normal responses; Abnormal responses; Clinical case study workshop.

5:30—Dinner.

Cost: $45.00. Contact: Quinton Seminars, 2121 Terry Avenue, Seattle, WA 98121.

University of Minnesota

Neuro-Muscular Dysfunction of the Lower Urinary Tract, June 3-5, 1976. Differential diagnosis of psycogenic and organic dysfunction will be included, as will enunessis, stress incontinence, neurogenic bladder and incontinence in aging. Contact Director, Office of Continuing Medical Education, University of Minnesota, Box 293, Mayo Memorial Building, Minneapolis, Minnesota 55455.

Acute Phase of Myocardial Infarction

Prehospital Management of the Coronary Patient

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S. W. WEBB, B.Sc., M.B., M.R.C.P.*

A prehospital coronary care scheme is described. The mobile coronary care unit allows coronary care to reach patients soon after the onset of symptoms at a time when the risk is greatest. The high incidence of autonomic disturbance is probably associated with the early electrical instability of the myocardium and thus the high incidence of sudden death. Early coronary care not only makes possible the correction or prevention of ventricular fibrillation outside hospital but by diminishing the incidence of shock and pump failure it reduces further the mortality from acute myocardial infarction.

SIXTY-THREE PERCENT of deaths from acute myocardial infarction among males aged 50 or less occur within one hour of the onset of symptoms.[4] The majority of deaths, therefore, occur before hospital admission. It has been shown that the majority of these deaths are due to ventricular fibrillation.[2] In view of this high incidence of early sudden death it seemed logical to concentrate on the prehospital phase of the disease.

Prehospital Coronary Care Scheme

A mobile coronary care unit (MCCU) was started in Belfast in January, 1966.[20] The MCCU carries the usual equipment found in a hospital coronary care unit, monitoring apparatus, drugs, intravenous solutions, a battery operated DC defibrillator, and pacing catheters. All equipment is portable.

The family doctors were made aware of the problem of coronary deaths outside hospital and given a special telephone number which allowed a rapid response from the coronary care unit. A team, intern or resident or fellow and nurse both trained in coronary care, is able to reach more than 50% of patients within ten minutes of the receipt of a call from the family doctor or lay individual. The family doctor may activate the mobile unit if a message he has received from a patient, or from the individual with him, suggests the likelihood of acute infarction. Emergency calls from lay individuals are received by the hospital coronary care unit and assessed by the doctor on call.

When the mobile team arrives, monitoring is commenced and therapy continued in the patient's own home or at the site of attack. After pain has been relieved and a stable rhythm established the patient is moved into the MCCU. Monitoring is continued during transport. Haste or fuss during transit is most carefully avoided. Direct transfer from the MCCU to the hospital coronary care unit is ensured with monitoring continued during this transfer. The hospital emergency room is bypassed since many early deaths from myocardial infarction occur in this area of the hospital.

In the five-year period (1966-1970) the mobile unit made 3,882 calls, 21 patients refused hospitalization. Of these patients 1,614 (42%) had acute myocardial infarction; (acute myocardial infarction is defined as: (a) indubitable evidence of recent infarction or (b) sequential ST and T wave changes accompanied by significant and transient rise in enzymes or (c) left bundle branch block with similar enzyme changes). The diagnosis among 1,283 patients (33%) was acute coronary insufficiency. In 444 patients (12%) the emergency was not related to acute coronary disease, while unjustified calls amounted to 5% of the total. Forty-one of the 1,614 (2.5%) with acute infarction were transferred from other hospitals, usually because of acute atrio-ventricular block requiring pacing. There was no arrhythmic death in transit during the five year period.

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*Cardiac Department, Royal Victoria Hospital, Belfast, N. Ireland.

First Hour of Acute Myocardial Infarction

It has been said that those who die within one hour seldom have the opportunity to obtain medical attention.[9] It has also been said that it is difficult to conceive that under any system much can be done about them. This view is unduly pessimistic. Where general practitioners are aware that the majority of coronary deaths are unnecessary and when a MCCU exists 28% of patients managed by such a unit will obtain intensive care within the hour.[20,3]

Over the past six years we have seen 652 patients within one hour of the onset of acute myocardial infarction. In the majority of these the initial observations were made outside hospital. Eighty-seven developed a myocardial infarction in hospital or reached the casualty department within one hour. Since clinical observation of patients seen within one hour might yield information regarding the factors precipitating ventricular fibrillation, a detailed prospective study was made of the last 294 of the 652. These 294 patients were seen between September 1970 and February 1973. These patients had from the time of the initial observation continuous recording of the electrocardiogram and frequent estimations of the blood pressure. One hundred and thirty-eight patients had anterior infarction, 147 posterior infarction, and nine had left bundle branch block or combined anterior and posterior infarction. In 111 of the 294 patients the interval between the onset of symptoms and the initial observation was less than 30 minutes.

Rhythm Disturbances

There was a high incidence of dysrhythmias among the patients in this prospective study (Table 1). Forty percent had bradyarrhythmia within the first four hours of the onset of symptoms. Bradyarrhythmia was most frequent among patients with posterior infarction. Ventricular ectopics occurred in 93% within the first four hours.

Primary ventricular fibrillation occurred in 55 of the 294 patients (Figure 1). Forty-one (75%) of the 55 had ventricular fibrillation within two hours of the onset of symptoms. Twenty-three of the 55 had ventricular fibrillation before the mobile team arrived; ten survived to leave hospital. Those who developed ventricular fibrillation did so without warning dysrhythmias or despite apparently adequate antiarrhythmic therapy.

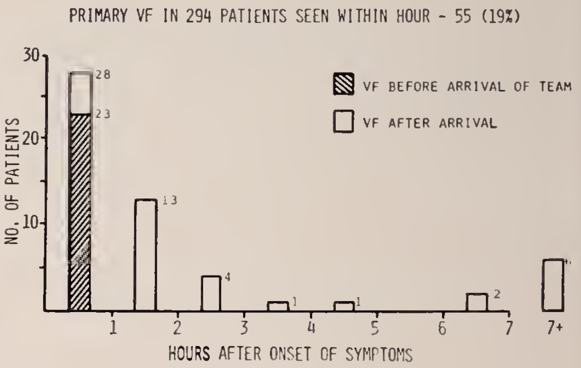

Fig. 1—Incidence of primary ventricular fibrillation in 294 patients seen within one hour.

TABLE 1

Incidence of Dysrhythmias within Four Hours among 294 Patients Seen within the First Hour

Dysrhythmia		No. within 1st Hour	No. within 2nd	No. within 3rd and 4th	Total within 4 Hours
Bradyarrhythmia	(248)	84 (34%)	9 (3.5%)	7 (2.5%)	100 (40%)
Ventricular Ectopics	(294)	171 (58%)	80 (27%)	24 (8%)	275 (93%)
Ventricular Fibrillation	(294)	28 (9.5%)	13 (4.5%)	5 (1.5%)	46 (15.5%)
Ventricular Tachycardia	(294)	6 (2%)	4 (1.5%)	1 (0.5%)	11 (4%)
Supraventricular Dysrhythmias	(266)	4 (1.5%)	7 (2.5%)	5 (2%)	16 (6%)

Figures in brackets indicate the number of patients in whom assessment was possible.

Autonomic Disturbance

Documentation of the autonomic disturbance at the time of initial observation was attempted. This was not possible in patients who presented with ventricular fibrillation or in those who had been on hypotensive drugs or beta-blocking agents prior to the onset of infarction. Patients showing left bundle branch block or combined anterior and posterior infarction were also excluded. Analysis of the autonomic disturbance was, therefore, confined to 240 of the 294. Eighty-nine of the 240 were seen within 30 minutes. Forty-four of the 89 had anterior infarction and 45 posterior infarction.

Patients with sinus tachycardia (heart rate 100 or more) with or without transient hypertension (blood pressure 160/100 mm Hg or higher) were considered to show sympathetic overactivity. Transient hypertension in the absence of sinus tachycardia was also regarded as evidence of sympathetic overactivity.

Patients with sinus or nodal bradycardia (heart rate 60 or less) or atrioventricular block (second degree or complete) were considered to show parasympathetic overactivity. Transient hypotension (systolic blood pressure 100 mm Hg or lower) in the absence of bradycardia was also regarded as evidence of parasympathetic overactivity.

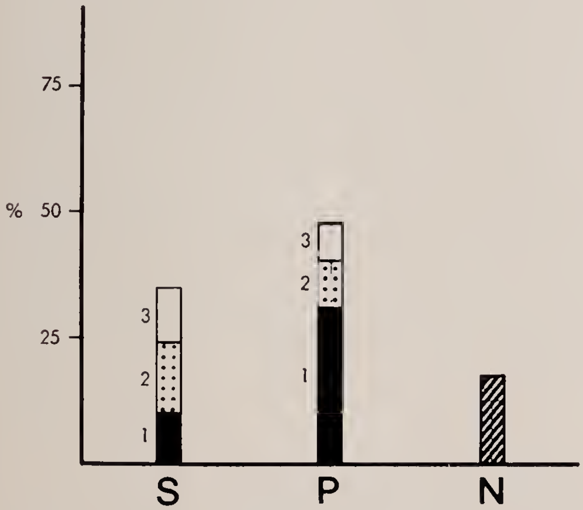

Fig. 2—Evidence of autonomic disturbance in 89 patients seen within 30 minutes. S = Sympathetic overactivity. S1 = Sinus tachycardia with hypertension. S2 = Sinus tachycardia. S3 = Transient hypertension. P = Parasympathetic overactivity. P1 = Bradyarrhythmia with hypotension. P2 = Bradyarrhythmia. P3 = Transient hypotension. N = normal heart rate and blood pressure.

Among the 89 patients seen within 30 minutes only fifteen (17%) had a heart rate and blood pressure within the normal range at the initial examination (Figure 2). Thirty-one (35%) showed evidence of sympathetic overactivity. Twenty-one of the 31 had sinus tachycardia, accompanied in nine by hypertension. Ten had transient hypertension with a normal heart rate. Parasympathetic overactivity was present in 43 (48%). Thirty-six of the 43 had bradyarrhythmia, 28 with associated hypotension. Seventeen (47%) of the 36 patients with bradyarrhythmia had a systolic blood pressure not greater than 80 mm Hg. Seven of the 80 had complete atrioventricular block, all with a systolic blood pressure 80 mm Hg or less. In a further seven patients transient hypotension (range 0-90 mm Hg) occurred in the presence of a normal heart rate and normal atrioventricular conduction.

The autonomic disturbance among patients with anterior infarction differs from that occurring in association with posterior infarction (Figure 3).

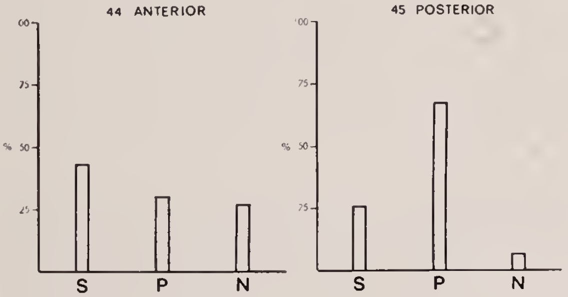

Fig. 3—Autonomic disturbance among patients seen within 30 minutes; 44 with anterior infarction and 45 with posterior infarction. Key as for Figure 2.

It can be seen that of patients with posterior infarction over two-thirds had vagal overactivity at the initial observation. Among the patients with a posterior infarction who had not had a previous infarction, evidence of parasympathetic overactivity was present in 20 of 21 patients (95%). The incidence of autonomic disturbance was significantly lower ($p = < 0.001$) in the 151 patients seen within the second half of the first hour (Figure 4). Sixty-six patients (44%) had a normal heart rate and a normal blood pressure. Sympathetic overactivity was observed in 41 (27%) and parasympathetic overactivity in 44 (29%).

Various mechanisms have been cited to explain

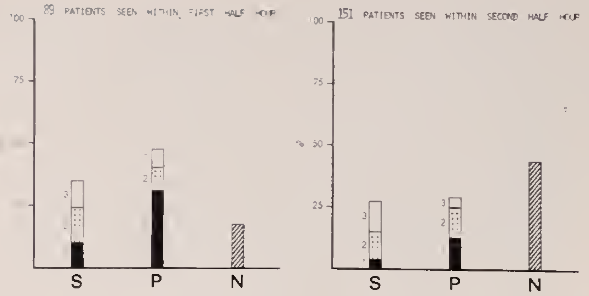

Fig. 4—Key as for Figure 2.

the early bradycardia and its usually associated hypotension. More than a century ago Von Bezold described a cardiogenic reflex precipitating bradycardia and hypotension.[5] Stimulation of the vagal neuroreceptors in the region of the coronary sinus and atrio-ventricular node may produce the human counterpart of the Von Bezold-Jarisch reflex.[13] The anatomical distribution of these vagal receptors may be the reason for the greater frequency of bradycardia in patients with a posterior myocardial infarction. The bradycardia and hypotension usually respond to atropine.[1] We have shown that early acute atrio-ventricular block complicating posterior myocardial infarction will respond to atropine in most cases[1,27] (Figure 5). Atrio-ventricular block may result from vagal overactivity in the absence of marked slowing of the atrial rate. When atrio-ventricular conduction disturbance is associated with block of the right coronary artery the obstruction is in the majority of cases distal to the origin of the sinus node artery. One of the effects of ischemia may be interference with cholinesterase activity.[8] This may lead to an accumulation of acetylcholine in the region of the atrio-ventricular node. Thus, the bradycardia associated with atrio-ventricular block may require a relatively large amount of atropine for its correction. The profound hypotension which may be associated with bradycardia complicating clinically acute myocardial infarction may be related not only to the inability of the damaged myocardium to increase stroke volume in the presence of a slow heart rate but also to the known loss of atrial transport function which results from vagal stimulation even in the absence of atrio-ventricular block.[25] In addition, vagal overactivity exercises a negative inotropic effect on the ventricle.[7,28] Among 89 patients seen within 30 minutes, 36 had bradycardia. Twenty-eight (78%) of these had bradycardia and hypotension. In seventeen (47%) of the 28 systolic blood pressure was not above 80 mm Hg. Indeed, three of these seventeen had an unrecordable blood pressure and the average systolic blood pressure of the remainder was 73 mm Hg. It is likely that the

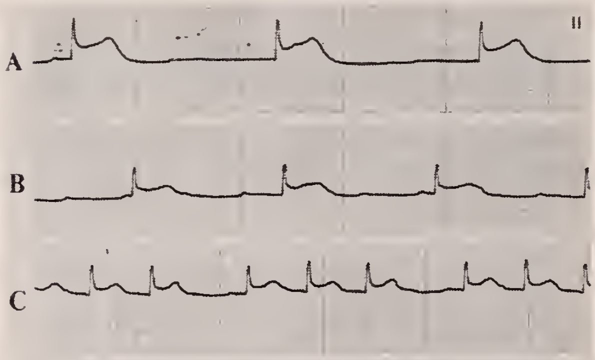

Fig. 5—(A) Atrial rate 52 per minute; ventricular rate 31 per minute. Blood pressure unrecordable. (B) Two minutes after atropine 0.6 mgs. Atrial rate 105 per minute; ventricular rate 40 per minute. Systolic blood pressure 75 mm. Hg. Reduction in ST segment when compared with A. (C) Three minutes after atropine 1.2 mgs. Second degree A.V. block. Atrial rate 115 per minute; ventricular rate 88 per minute. (D) Four and a half minutes after atropine 1.2 mgs. Normal A.V. conduction; PR interval 0.2 second. Ventricular rate 110 per minute. Blood pressure 170/110 mm. Hg.

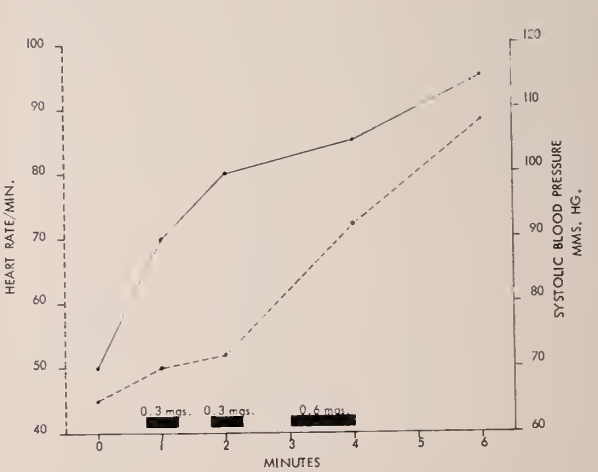

Fig. 6—Sinus bradycardia and hypotension at an estimated 50 minutes after the onset of acute posterior infarction. The effect of three aliquots of intravenous atropine total 1.2 mgs.

mean arterial pressure of most of these patients was considerably less than 70 mm Hg. At this coronary perfusion pressure blood flow through the ischemic zone is likely to be minimal[18,19] and blood flow through previously non-ischemic myocardium is likely to be less than adequate.[18] A marked improvement in the haemodynamic situation may be obtained from a small amount of atropine producing a limited rise in heart rate (Figure 6). In the example shown a rise in heart rate from 45 to 52 was associated with a rise in systolic blood pressure from 70 to 100 mm Hg, presumably because of improved atrial function and reduction in the negative inotropic effect of the vagal activity on the ventricles. Indeed, in 80% (28 of 35) both the bradycardia and hypotension occurring immediately after the onset of acute myocardial infarction responded to atropine (Table 2). Only three of the 23 patients with sinus bradycardia failed to show a rise in blood pressure in association with the rise in heart rate. Among the twelve patients with complete atrioventricular block, eight responded to atropine with an improvement in atrio-ventricular conduction and correction of the hypotension. In one the rise in blood pressure did not accompany the rise in heart rate. Atropine had no effect on either blood pressure or heart rate in three of the twelve.

Not only is the bradycardia hypotensive complex of acute myocardial infarction of significance in relation to the reduction in coronary blood flow but the relationship of bradycardia to ventricular dysrhythmias is important. It is well known that ectopic beats may appear as the heart rate slows. Vagal overactivity in association with myocardial infarction may be profound and may precede the appearance of ventricular tachycardia (Figure 7) or ventricular fibrillation. In the clinical situation vagal and sympathetic overactivity may co-exist.[27] It is known that relatively weak vagal overactivity usually overpowers even strong sympathetic overactivity.[24] Sympathetic overactivity may be unmasked by the correction of vagal overactivity.

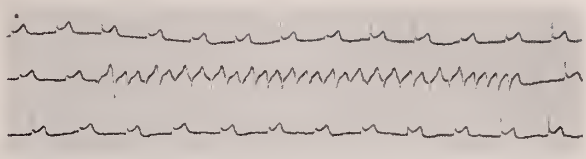

Fig. 7—Acute posterior infarct, lead two. Nodal bradycardia with unrecordable B.P., self-terminating ventricular tachycardia/ventricular flutter. (Continuous record in patient's home.)

While vagal overactivity in relation to acute myocardial infarction, both clinical and experimental, has been the subject of much comment less attention has been paid to sympathetic overactivity. The data presented here indicate that clinical evidence of sympathetic overactivity was present in 31 (35%) of 89 patients with acute myocardial infarction seen within an estimated 30 minutes and in a further seven (8%) sympathetic overactivity was unmasked by correction of vagal overactivity. Tachycardia may have an adverse effect on the ischemic area surrounding the infarct.[16] Increase in the heart rate in the presence of ischemia has been shown to cause a fall in the ventricular fibrillation threshold.[14,12] Ventricular fibrillation may appear following spontaneous increase in the heart rate (Figure 8). It may also

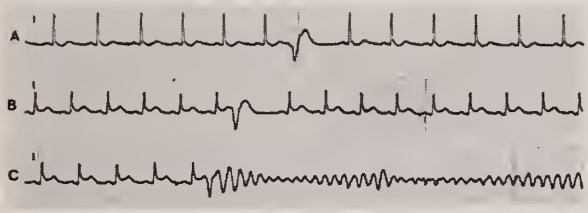

Fig. 8—Lead 1, anterior infarct, estimated 55 minutes after onset of chest pain. (A) Sinus rhythm (rate 95). Occasional 'benign' ventricular ectopics. (B) Four minutes later, sinus tachycardia (rate 110) with ST segment elevation 1.0 mm. (C) One minute after B, development of ventricular fibrillation before treatment could be given.

TABLE 2
Effect of Atropine in 35 Patients with Bradyarrhythmia and Hypotension Seen Within the First Hour

	Atropine given for bradyarrhythmia and hypotension	Rise in rate and blood pressure	Rise in heart rate only	No effect
Sinus Bradycardia	23	20	3	0
A.V. Block, second degree or complete	12	8	1	3
Total	35 (100%)	28 (80%)	4 (11%)	3 (9%)

follow inappropriate increase in the heart rate produced by atropine. In the control of sympathetic overactivity, overt or unmasked, practolol was used in aliquots of 5-10 mgs intravenously. The maximum total dosage was 20 mgs. Sotalol in aliquots of 10 mgs was found to have a more potent negative chronotropic effect than practolol. Reduction in the ST segment elevation usually accompanied fall in heart rate (Figure 9). This fall in the ST segment is likely to indicate reduction in the ischemia in the area surrounding the infarct.[16]

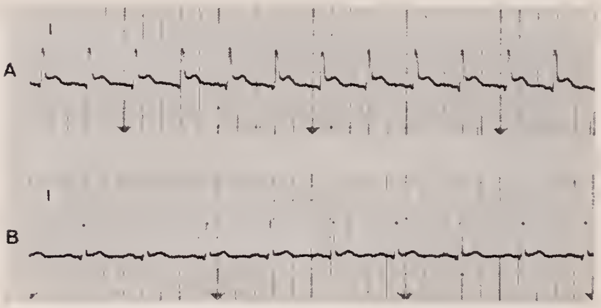

Fig. 9—Effect of sotalol on sinus tachycardia in a normotensive patient with anterior infarction. Lead 1 (10.2.73) recorded an estimated 40 minutes after onset of infarction. (11.2.73, CPK 436, SGOT 127). (A) Sinus tachycardia (rate 125). ST segment elevation 2.5 mm. (B) Six minutes after sotalol 10 mgs. intravenously: rate 96, ST elevation 0.5 mm.

It has been shown that the magnitude of the area of infarction and thus the incidence of shock and pump failure may be reduced by the early initiation of intensive care.[21]

Effectiveness of Lidocaine

The high incidence of autonomic disturbance in the very early phase of acute myocardial infarction may explain the limited response to lidocaine observed at that time. We presented in 1970 data suggesting that lidocaine is of limited value in the control of ventricular dysrhythmias occurring within one hour of the onset of infarction.[22] At that time lidocaine abolished ventricular ectopic activity completely in only 27% and in 38% it had no effect. Our subsequent studies have shown that lidocaine may be without effect even in the presence of relatively high blood levels of the drug (Figure 10). The effect of lidocaine in suppressing ventricular ectopics may be rate related. We have found lidocaine less effective in the presence of sinus tachycardia (Figure 11). When the heart rate was over 90 ectopic activity was diminished or abolished in only 31% and was unaffected or increased in 69%. In view of the limitations of lidocaine in the presence of tachycardia its effect on the heart rate was investigated. The drug caused a rise in the rate of ten per minute or more in 22% of patients when given in the standard dosage (Figure 12). This rise in the heart rate may interfere with antiarrhythmic action of the drug. However, in the absence of sinus tachycardia when the heart

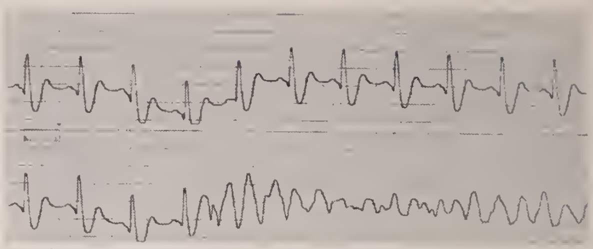

Fig. 10—Onset of ventricular fibrillation in a patient with acute anterior infarction despite blood lidocaine level of 3.3 μg/ml.

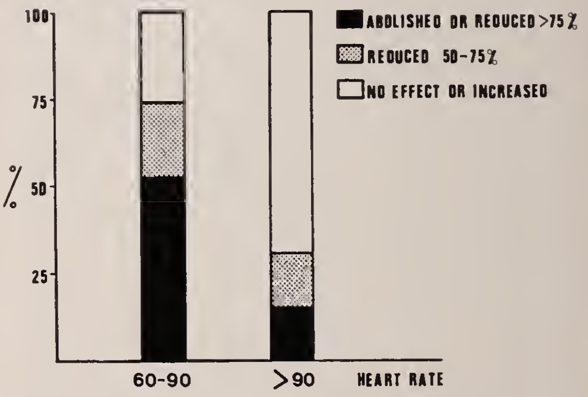

Fig. 11—The effect of lidocaine 100 mgs. intravenously followed by an infusion of 2 mgs/min. on ectopic activity in 24 patients (heart rate 60-90) compared with its effect in 12 patients (heart rate over 90). The difference is highly significant.

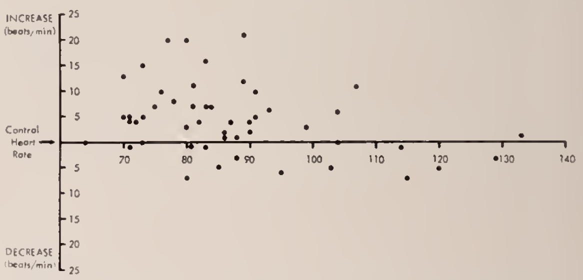

Fig. 12—Effect of lidocaine 100 mgs. intravenously followed by an infusion of 2 mgs/min. on the heart rate in 49 patients with acute myocardial infarction. Average heart rate five minutes before and five minutes after start of lidocaine (cannula in situ before estimation of control heart rate).

TABLE 3

	Patients Under 70 Years	Shock	Mortality
Prospective Study (1970-1973)	271	9 (3.3%)	27 (<10%)
Bristol Study (1971)	117	Not recorded	30 (25.6%)

rate was between 60 and 90 the drug had a beneficial effect on ectopic activity in 74% of patients and had no effect or increased the ventricular dysrhythmia in 26% (Figure 11). The contrast between the limited value of lidocaine in the early prehospital phase of acute infarction and its effectiveness in the coronary care unit suggests that early ventricular dysrhythmias may differ from those that occur later.[23] There is evidence that early ventricular dysrhythmias are re-entry in origin.[26,10,15] Those that occur later may result from increased automaticity.[15] Lidocaine decreases the slope of phase four of the action potential[6] and might be expected to abolish ventricular dysrhythmias due to increased Purkinje automaticity. The effect of lidocaine on re-entrant dysrhythmias is much less predictable. Enhanced re-entry produced by lidocaine has been demonstrated in dogs.[11]

A possible approach to the problem of ectopics which are frequent, multifocal, or R on T in type, is the use of lidocaine in adequate dosage, at least 100 mgs intravenously followed by 2 mgs per minute or more when the rate is 60-90. Ectopic activity in patients with heart rates above 90 might be managed by reducing the rate with a beta-blocking agent. Lidocaine might then be administered if required.

Effect of Early Care on Hospital Mortality

Therapeutic intervention in the acute phase of myocardial infarction appears rewarding. The mortality among our 271 patients aged 70 years and less seen and treated within the first hour was less than 10% which is to be compared with a mortality of almost 26% among patients in the Bristol study[17] who sought medical advice within one hour (Table 3) but who presumably received no treatment.

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23-28. Will be found on page 346.

Classified Advertisements

(Continued from page 325)

THE FARIBAULT CLINIC LTD., has an immediate opening for a Family Physician and a General Surgeon who is Board certified or eligible. The Clinic is in a rural community near the metropolitan area and consists of six Family Physicians, one Surgeon and two Internists. For information please write to: Mrs. Arlene Pfeffer, Faribault Clinic Ltd., 924 N.E. 1st St., Faribault, Minnesota 55021.

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PHYSICIAN'S ASSISTANT available June 1976. 32 year old, ex-Navy Corpsman, BS Purdue 1974, BS Physician's Assistant Program, College of Medicine, University of Iowa, 1976. Seeking rural GS, FP, or Peds. Resume on request. J. David Girard, RR #5, Box 213, Rensselaer, Indiana 47978.

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WANTED—CHILD PSYCHIATRIST or Psychiatrist to join a well established four man group located in University community of 46,000 with a large referral area. We have two excellent hospitals. Community is 90 miles from Twin Cities. Salary is open. For further information contact E. R. Brousseau, M.D., Northwest Psychiatric Clinic, Eau Claire, Wisconsin 54701. Telephone: 715-834-2751.

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Anderson, C. F., Co. 310
Burroughs-Wellcome Co. 329
Blue Shield/Blue Cross 320
Classified Advertising 325
Dahlberg Hearing Aids 286
Finley & Friday, Inc. 318
Flint Laboratories 330, 331, 332
Fredrick Herfurth Real Estate, Inc. 340
Kjell Bergh Borton Volvo, Inc. 288
Lilly, Eli, & Co. 296, 340
Medical Protective Company 288
North Central Medical Conference 316
Pharmaceutical Mfrs. Assn. 338, 339
Ramada Inn 328
Robins, A. H. Company 323, 324
Roche Laboratories .... Cover 2, 285, 310, 311, Cover 3, Cover 4
Roerig and Company 314
Smith, Kline & French 312
Volvo, Kjell Bergh's Borton 288
U.S. Navy Recruiting 290
Upjohn Company 313

Blinding Hockey Injuries

Dr. Richard Horns has requested that we publish the following correction to his article, page 257, last paragraph, right-hand column, April issue:

> It is the recommendation of the Committee on Ophthalmology of the Minnesota State Medical Association that persons playing hockey wear an eye protective device. In particular, it is the feeling of the Committee that Minnesota statute **requires** (should require) all students taking part in school hockey programs to wear an eye protective device.

Children's Hospital

The Department of Newborn Medicine of St. Paul Children's Hospital is offering a refresher course in Neonatal Resuscitation and stabilization for obstetricians, pediatricians and family physicians. The one-half day program will consist of discussions and demonstrations in areas of: delivery room resuscitation and stabilization, pediatric surgical problems of the first hour of life, radiologic diagnosis during the first hour of life and instruction in endotracheal intubation using animal models. The course will be limited to six participants, and will be offered the last Thursday of every month at St. Paul Children's Hospital. Tuition is $10 per participant. For further information, contact either Dr. Steve Boros or Bernadette Zollner, St. Paul Children's Hospital. 311 Pleasant Avenue. St. Paul, Minnesota 55102, 227-6521 X390.

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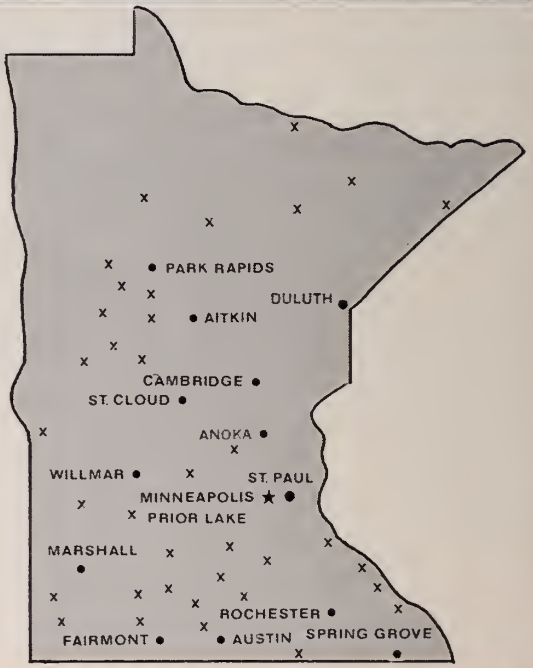

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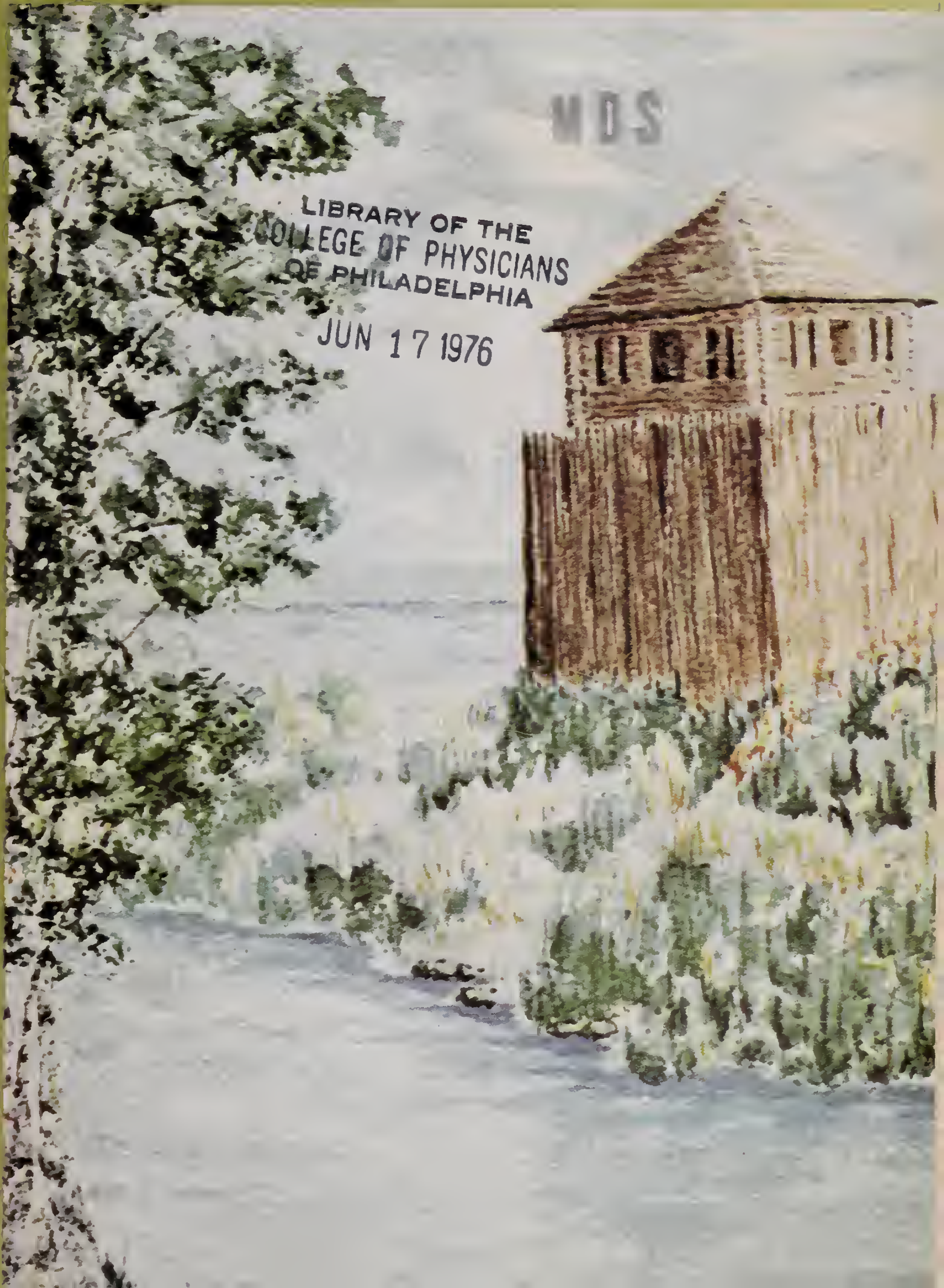

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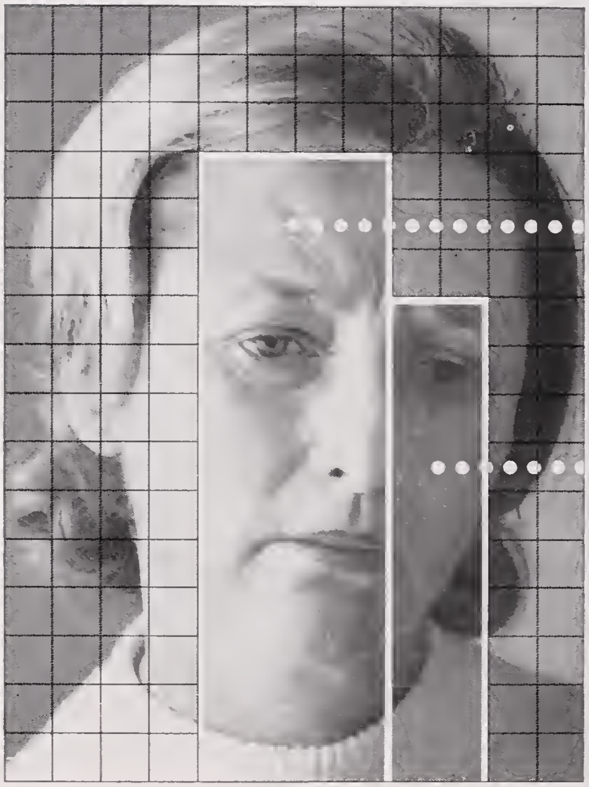
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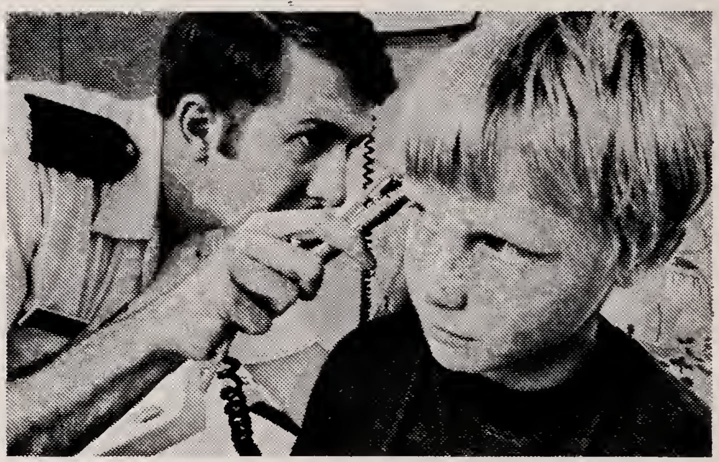

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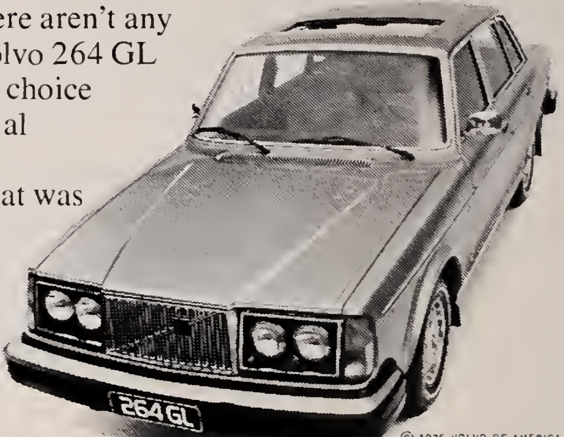

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President's Letter

A Tribute to Roy Diessner

The most enjoyable job of an incoming president is the opportunity to publicly give final recognition and extend heartfelt thanks to our retiring president, Roy Diessner. At our last council meeting I sat next to Roy and observed, following 13 hours of continuous deliberations on important Minnesota medical affairs, a physically and mentally exhausted president. This meeting was a culmination of a year of travel, speeches, legislative testimony, meetings, ceremonial events, and, lastly but most important, absence from his family, friends, and medical practice.

His devotion and dedication to the duties of president of our State Medical Society have been an inspiration to those of us who will follow. He served with dignity, wisdom, and a wealth of experience. He was informed, articulate, and patient in his approach to the difficult medical and socio-economic problems that we have faced the past year.

First and foremost Roy is a highly capable physician representing with excellence, one of the world's great medical centers, the Mayo Clinic. He served efficiently in his county medical society, then as a delegate to the State Medical Society, as a councillor and finally as chairman of the Council before assuming the office of president.

We salute him now and record our thanks for the service he has rendered.

Richard E. Anonsen, M.D.
President
Minnesota State Medical Association

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Editor's Notebook

Editor's Report to the House of Delegates

When I became Editor on January 1, 1975, I had these goals: (1) to produce a good journal, (2) to do this well enough to give the Journal added prestige, and (3) to make the Journal as financially self-sufficient as I could.

Well, a year has passed. The time has come to judge how well we have done. I use the editorial "we" here to include myself, the Board of Editors, and Doctor Elaine Nye. Elaine, as you may know, supplies the glue that binds the whole enterprise together.

How well have we accomplished these goals? I cannot directly judge our performance on the first two goals, for it's up to the readers to decide how good the Journal is and how our prestige rates. But I can throw in a couple of indirect observations: (1) the newspapers, particularly those in the Twin Cities, have quoted us or commented on MINNESOTA MEDICINE on at least ten occasions this year indicating the media respects our opinion; and (2) a reader's questionnaire in the November issue of MINNESOTA MEDICINE got a lively response, indicating about 70 per cent of the readers read half the articles. I consider that a respectable half-life for a medical journal.

Our success in achieving the third goal—financial self-sufficiency—is something that can be measured. There are limits, of course, to how economically self-reliant we can be, but we're going in the right direction. In 1975 *three percent* of your annual dues went to run the Journal, while in 1974 the figure was *five percent.* In part, of course, this proportional decrease occurred because your dues climbed $100 a year.

But four other major factors were also involved: (1) we cut our number of printed pages from 895 to 794, a decline of 11 percent; (2) we increased our local advertising from $5,997 to $7,953, a rise of 33 percent; (3) our national advertising revenue went from $23,483 to $28,417, an increase of 21 percent; and (4) our reprint income leaped from $9,427 to $14,386, a jump of 53 percent.

In other words, we pulled in our belt and went after the advertising and reprint revenue. As a result, we finished $1,163 under our budget of $40,000. For perspective, you may wish to compare this performance to other years:

Year	Budget	Financial Picture
1972	$40,000	$8,967 under budget
1973	40,000	219 under budget
1974	40,000	8,720 over budget
1975	40,000	1.163 under budget
1976	44,000	now under budget
1977	46,000	request for 1977 (to be approved by the House of Delegates)

Note that we are now running under budget through April 1. This is again due to our lean issues and increased revenue. Here, for your information, is how we're doing with local and national advertising the *first three months of 1976,* compared to 1975:

	First Three Months of Year		Percent Increase
	1975	1976	
Local Ads	$ 833	$1,851	122% increase
National	$8,176	$8,583	5% increase

Given these figures, why am I asking for a $2,000 increase in our 1977 budget? Partly to hedge against future inflation, but also, because I have three projects in mind for 1976 that may bring us close to the $44,000 figure. These are: (1) Four to six bicentennial articles relating to Minnesota's role in American Medicine these last 200 years, (2) a monthly article from the Division of Socio-economic Affairs, and (3) a series of personal interviews with the political leaders of the Minnesota State Medical Association. I feel MINNESOTA MEDICINE has a role to play in the political process. The purpose of these interviews is to convey political messages from our leaders to our members. An interview is a comfortable way to do that, and I think the readers will find the interview readable. At this writing, we have already conducted one of these interviews with Dr. Richard E. Anonsen, our president, and Doctor Roy Diessner, our immediate past-president, has agreed to be interviewed. I know you will agree these three projects are worthwhile.

Richard L Reece MD

Editor-in-Chief

Contents—June, 1976

Volume 59, 6
Pages 357-434

COVER PAINTING—"Old Fort at Grand Portage"
Tague Chisholm, M.D. 397

PRESIDENT'S LETTER—A Tribute to Roy Diessner
Richard E. Anonsen, M.D., President 361

EDITOR'S NOTEBOOK—Editor's Report to the House of Delegates
Richard L. Reece, M.D., Editor-in-Chief 363

ORIGINAL CONTRIBUTIONS

Tennis Elbow
James D. Priest, M.D. 367
Congenital Left Ventricular Diverticulum
Laura Knight, M.D. et al 372
Management of Intra-Abdominal Henoch-Schönlein Purpura
Luis H. Toledo-Pereyra, M.D. et al. 376
"Silent Thyroiditis" Versus Thyrotoxicosis Factitia
Fred D. Hofeldt, M.D. et al. 380

INTERVIEWS—An Interview with Richard E. Anonsen, M.D.
President of the Minnesota State Medical Association 383

EDITORIALS

Michigan Alcoholic Screening Test
Richard O. Hellman, M.D. 395
Erosion of Indian Mental Health in Cities
James D. Swenson, M.D. 395
Twenty-Five Years Association of a Psychiatrist
John A. Haugen, M.D. 397

LETTERS TO THE EDITOR

Preventive Medicine
Earl T. Carter, M.D. 399
I Almost Saw a Bear
John E. Smith, M.D. 401
Attitudinal Barriers Towards the Physically Disabled Person
Leah J. LaBar 403

FIFTY YEARS OF FAITHFUL SERVICE 405

LEGISLATION—If We Had Not Been There
C. A. Anderson, M.D., Chairman, Committee on Public Policy 407

GRAND ROUNDS—Heat Sroke
Roger Ralston, M.D. 411

REHABILITATION—Infant/Preschool Hearing Impaired Child
Winifred H. Northcott, Ph.D. 419

ADDICTION—The Routine Administration of the Michigan Alcoholic Screening Test to Ambulatory Patients
Robert B. Breitenbucher, M.D. 425

Mental Health—Erosion of Indian Mental Health in Cities
Joseph Westermeyer, M.D. 431

CLASSIFIED ADVERTISEMENTS 406

INDEX TO THE ADVERTISERS 434

MINNESOTA MEDICINE REPRESENTS

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Tennis Elbow

The Syndrome and A Study of Average Players

JAMES D. PRIEST, M.D.*

This is the first of two articles on elbow injury in tennis players. In an upcoming issue of Minnesota Medicine a study of world caliber tennis players performed by Dr. James Priest and associates will be published.

THE RECENT BOOM in the popularity of tennis has led to an increase in the number of players sustaining injuries and seeking medical advice, and due to the stresses of the game, the elbow is a frequent site of complaint. Any pain about the elbow, whether in an athlete or not, has often been referred to as "tennis elbow" by the general populous. In truth, several places about the elbow may become painful, but there is only one "tennis elbow."

Symptoms

The symptoms of "tennis elbow" occur over the lateral humeral epicondylar area. Pain may be severe, tenderness may be exquisite in this one small area, and in an advanced case sharp discomfort is felt over the lateral epicondyle upon pronation and supination of the forearm, or on flexing and extending the elbow. In a most advanced case, the patient may be unable to pick up a teacup because of excessive pain over this region of the elbow.

Discomfort over the medial epicondyle is less common in tennis players, an area sometimes injured in Little League pitchers. The ulnar nerve courses between the medial epicondyle and the olecranon process, and trauma to or impingement of this nerve may cause pain in this region, or in a radiating pattern down the medial forearm and hand. The medial epicondyle and the ulnar nerve groove are affected in tennis players, but with less frequency than the lateral epicondylar region, and are not classically referred to as "tennis elbow."

Etiology

"Tennis elbow" is suffered by athletes and nonathletes alike. Carpenters, dentists, surgeons, or anyone involved in an activity or occupation requiring repetitive rotation of the forearm, or wrist flexion and extension, is prone to acquire lateral epicondylitis. While many authors have advocated changing the title of the condition, the name "tennis elbow" persists.

The first game of lawn tennis was played in Wales just over a century ago, and the first patient with lateral humeral epicondylitis was described in the same year (1873) in a writer, not a tennis player.[1] Despite hundreds of articles in the medical literature on the topic of "tennis elbow" over the past century, little progress has been made in establishing the precise etiology of pain over the lateral epicondylar region.

More than 25 lesions have been listed in the literature as the cause of lateral epicondylar pain. Bursitis, arthritis, and neuritis are among those mentioned. It is our impression that there are several causes of pain in this area of the elbow, the most common being a tendinitis at the point of origin of the common extensor tendon from the lateral epicondyle. No agreement exists, however, among experts in the field as to the exact etiology.

Therapy

That the cause of "tennis elbow" has remained a mystery is doubtless the reason that therapy for this condition has been highly variable. Friedlander, in 1967, listed 43 forms of conservative management for "tennis elbow" in the literature up to that time.[2] He included radiation, manipulation, rest, immobilization, local injection, systemic medication, and physiotherapy. To these may now also be added acupuncture, the hinged elbow brace described by Ilfeld,[3] and the proximal forearm band described by Froimson.[4]

---

*Minneapolis, Minnesota.

Non Elastic Cloth Strap

The proximal forearm band is a non-elastic cloth strap which is wrapped snugly about the bulkiest portion of the upper forearm. For moderately symptomatic patients it is worn during any period of activity, and for those who are highly symptomatic it is worn all of the time except at night. The mode of action of this appliance is presumed to be reduction in the pull of the common extensor tendon over the lateral epicondyle by reducing the capacity of the extensor musculature to fully contract. This device generally appears to reduce discomfort by a significant amount, but usually does not affect a cure.

Local Injection

Local injection into the region of maximal pain and tenderness is another common form of treatment. The injection is with a local anesthetic and an anti-inflammatory drug (steroid). The injection is closely followed by a period of 24-36 hours of increased discomfort, with subsequent resolution of pain for variable periods of time in different individuals. Persistent symptoms after a total of three injections should probably constitute a failure of this form of treatment.[5]

Systemic Drugs

Systemic anti-inflammatory medication, including aspirin, phenylbutazone, and oxyphenbutazone are also commonly prescribed.

Surgery

Surgical intervention is reserved for recalcitrant cases not responding to conservative management after one to two years. Fasciotomy of the lateral musculature, extensor tendon release, and orbicular ligament resection are among the procedures performed for persistent lateral epicondylitis.

Study of Average Tennis Players

Despite the volume of work done over the past century on the "tennis elbow" syndrome, surprisingly little has come forth on the treatment, or even the existence, of "tennis elbow" in the tennis player. In 1902, Clado,[6] studying several of the best players in France found lateral epicondylitis in tennis players, and thereby first connected the condition with the name it still carries. In the literature through the intervening years, however, "tennis elbow" has been associated infrequently with tennis players, and instead has been considered to be induced primarily by hobby or occupation.

Only recently, coincident with a recent surge in the popularity of tennis, has interest been rekindled in elbow injury in the tennis player. Chinn and Priest et al.[7,8] studied elbow changes and symptoms in highly skilled tennis players. Bernhang et al.[9] made a bio-mechanical study of "tennis elbow," and Nirschl[10] has discussed the etiology and treatment of "tennis elbow," both authors being primarily concerned with tennis players. However, since no statistical study characterizing "tennis elbow" in average tennis players has come forth, the following investigation was undertaken.

Material and Methods

Data were gathered by questionnaire from members of a northern California tennis club. An annual questionnaire regarding club activities was utilized. It was mailed to all members of the club, with questions about elbow injury falling at the end. Since virtually all who responded to the elbow questions did so after completing the major portion of the document, we feel our sample is not skewed towards players with or without symptoms. This primary portion of the investigation was designed to separate groups who did and did not develop pain. All players with symptoms were mailed a second more extensive questionnaire designed to further characterize the group with pain.

Two hundred and thirty-one players (132 males and 99 females) responded to the first questionnaire and are included in this study. Seventy-eight percent of those with pain responded to the second questionnaire, and each of these was in addition contacted personally by a member of the research team to determine the exact location of symptoms.

Multiple factors were investigated during this study, including conditions at the onset of pain, characterization of the pain, physical characteristics of the players, and equipment used by players both before and after the onset of discomfort. The data was transferred to punch cards and submitted for computer analysis.

Results

Location of Symptoms

Forty-seven percent of these average players had experienced elbow pain at some time during their tennis careers, and 28 percent had symptoms at the time of the survey. Seventy-five percent of the symptoms were over the lateral epicondylar region, 17 percent were on the medial side of the elbow, and eight percent were reported in various other locations.

Onset and Duration of Symptoms

Thirty-eight players reported a sudden onset of discomfort, and forty-five players a slow onset. If the onset was slow, the average length of time to the peak of pain was 1.8 months in the men and 1.6 months in the women. If the pain was episodic, the number of recurrences was approximately four for both men and women with an average duration per episode of three and one-half months in men and one month in women. If discomfort was reported as a single occurrence, its duration was usually about one year. In only 12 percent of cases was the weather reported as cold at the onset of pain, the remainder reporting warm or moderate conditions. Only 12 percent developed pain after a layoff from the sport.

Symptoms and Strokes

In the production of lateral epicondylar symptoms, the backhand stroke was implicated twice as frequently as the forehand or serve. However, of 11 players who used two hands on the backhand stroke, only one reported ever having had lateral epicondylitis, which in his case developed before using two hands and disappeared upon his changing to two hands. This finding suggests that the two-handed backhand may be protective or even curative of lateral elbow symptoms.

Frequency of Play

At the time pain was first noticed, the men were playing an average of 3.5 and the women 4.8 times per week. Figure 1 shows the percentage of players with elbow pain as a function of how often they played. Among those playing once or less per week, only 26 percent developed elbow pain. The percentage with pain rose steadily with increasing frequency of play to 54 percent among those playing six to seven times per week. Thus, in this study, the more frequently one played the more likely he or she was to develop pain.

Years of Play

In correlating the number of years played with the development of symptoms, we found that the proportion of players experiencing symptoms was around 35 percent for both men and women after

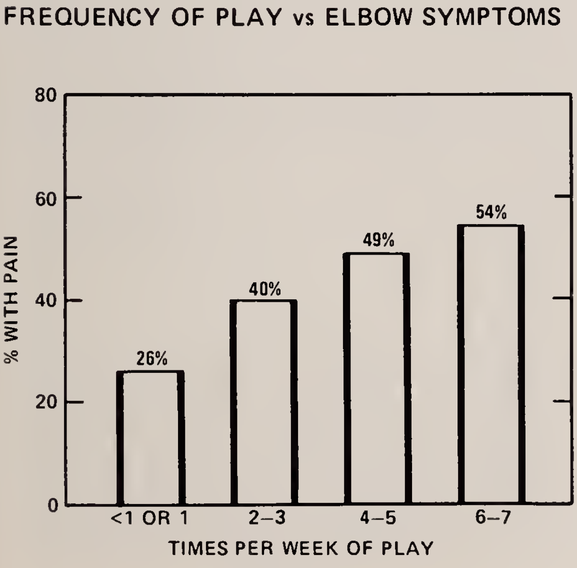

Figure 1

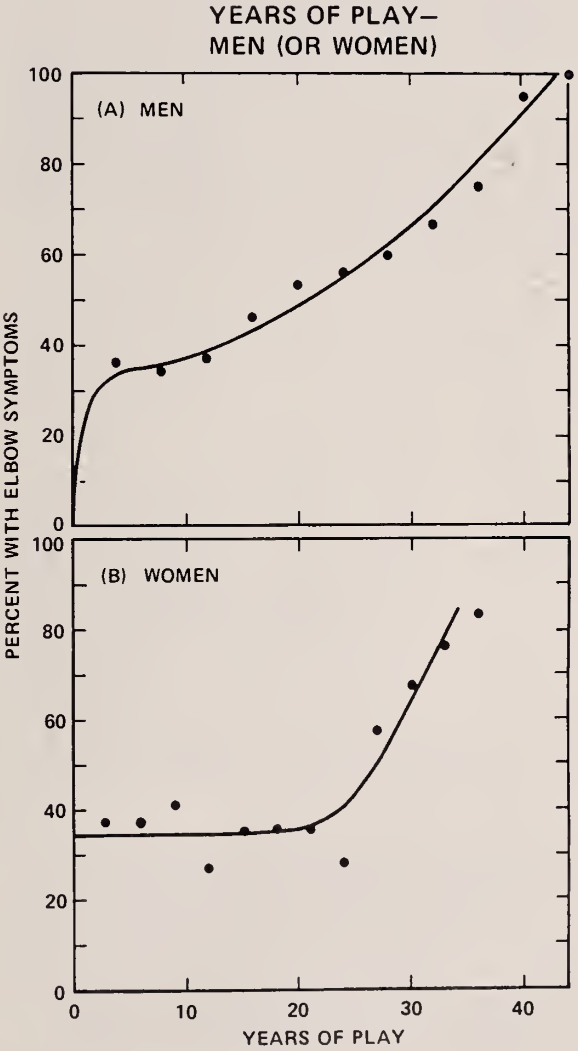

Figure 2

the first few years of play, and then gradually increased with years of play to 100 percent for men and 85 percent for women (Figure 2). Thus, in this study group, if one had played long enough, he or she had an extremely high probability of developing elbow symptoms at some point.

Years of Play and Frequency of Play

When multiplying years of play by frequency of play per week, the product was twice as great for the symptomatic group as the asymptomatic group. In other words, if symptomatic, a player had played tennis an average of twice as many times in his lifetime as his asymptomatic counterpart.

Level of Ability

With regard to the skill of the player and the likelihood of his developing symptoms, Figure 3 shows the percentage of players with elbow pain as a function of their class ranking in the club. In higher ranking players "tennis elbow" was more prevalent. This may merely indicate that better players play more frequently, and as a consequence develop more symptoms. These data would, however, tend to contradict the theories that beginners, weekend players, and lower ranking club players are the ones most likely to develop "tennis elbow."

SKILL vs ELBOW SYMPTOMS

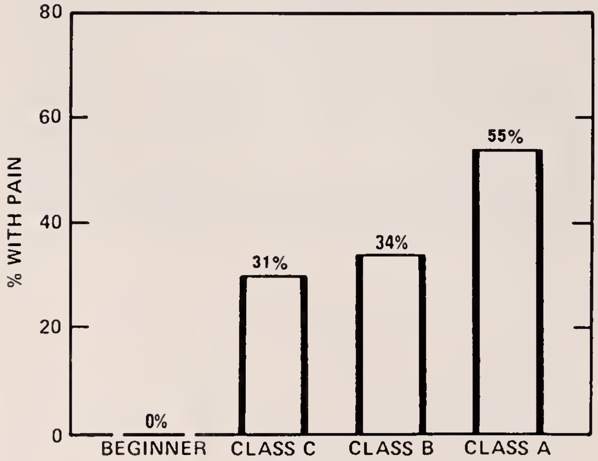

Figure 3

Cumulative Effects of Tennis

Based on the above findings with regard to frequency of play, years of play and player skill, it appears likely that any harmful effects of tennis may be cumulative over a period of time before elbow symptoms become manifest.

Equipment and Development of Symptoms

Equipment was analyzed with regard to the development of "tennis elbow" and the effect of racquet change after symptom onset. The following factors were considered: size, weight, and composition of racquet; and tension and composition of strings. For racquet weight, string tension, and string composition, no significant differences were found between the groups of players with and without symptoms. Table 1 shows that the average grip size was essentially the same for men and women with and without symptoms.

TABLE 1
Racquet Handle Size (Inches)

	Men	Women
With Symptoms	4.62	4.51
Without Symptoms	4.63	4.52

Racquet Composition

The most significant finding with respect to equipment was racquet composition. While approximately 50 percent of all players in this study used wooden racquets, 75 percent of those developing elbow symptoms were using a wood racquet at the time. Figure 4 demonstrates the relative

RACKET COMPOSITION—
MEN (OR WOMEN)

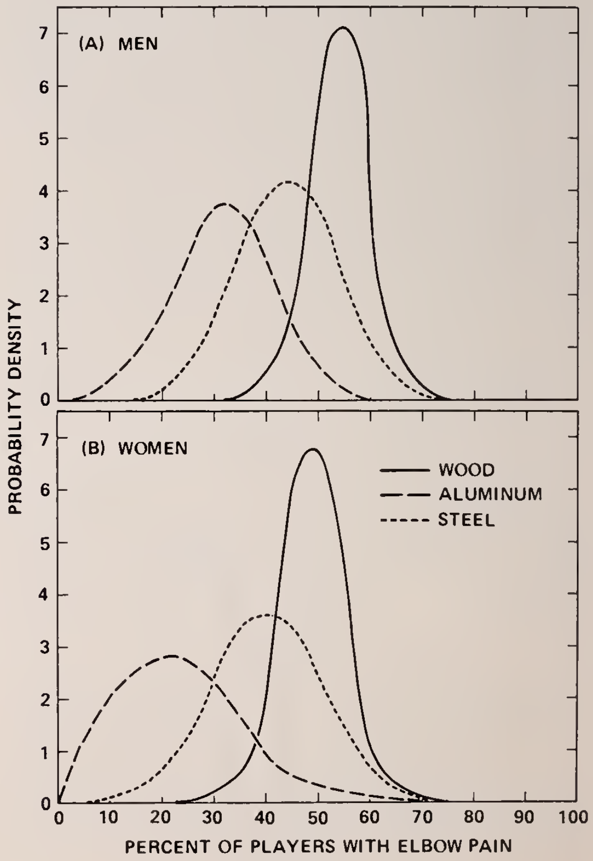

Figure 4

likelihood in our sample for developing elbow symptoms when using racquets of wood, aluminum, and steel. In both men and women the occurrence of symptoms was greatest for those using wood, followed by steel and aluminum in that order.

Improvement of elbow symptomatology after racquet change is demonstrated in Table 2. Among players who changed racquets after the onset of pain, 85 percent of those who changed from wood to another composition reported improvement, while of those who switched from one wood racquet to another, only 38 percent reported improvement. Over one-half of the unimproved players were among those who had changed from one wood racquet to another. Table 3 demonstrates that racquet composition was the parameter most frequently changed in the group of players whose symptoms improved after racquet change. While several parameters were often changed simultaneously when a new racquet was obtained, handle size, racquet weight, type of strings, and string tension do not appear to have been important in symptom reduction.

Summary

Forty-seven percent of the club tennis players in this study had elbow pain at some time. Seventy-five percent of the symptoms were over the lateral epicondylar region, with the backhand most frequently implicated. The more frequently one had played, the longer one had played, and the higher one's ranking in the club, the more likely was he or she to have developed elbow symptoms. The effects of tennis would thus appear to be cumulative over a period of time in the production of "tennis elbow." When various factors with regard to the racquet and strings were analyzed, racquet composition was found to be the most significant, with wooden racquets being more productive of symptoms than aluminum or steel.

A conservative regimen of treatment for the average tennis player might include use of the proximal forearm band (Froimson), a reduction in frequency of play, employment of the two-handed backhand, and change from a wood racquet to metal.

TABLE 2
Elbow Symptomatology
After Racquet Change (Number of Players)

Composition	Improved	Unimproved
Wood to Steel	22	4
Wood to Aluminum	6	1
Wood to Fiberglas	1	1
Steel to Wood	1	1
Steel to Aluminum	1	0
Aluminum to Wood	2	0
Steel to Steel	1	0
Wood to Wood	5	8

TABLE 3
Racquet Parameters Changed in Improved Group
(Number of Players)

Parameter	Changed	Unchanged	Undetermined
Racquet Composition		6	2
Wood to Steel	22		
Wood to Aluminum	6		
Wood to Fiberglas	1		
Steel to Wood:	1		
Aluminum to Wood	2		
Steel to Aluminum	1		
TOTAL	33		
Handle Size		22	0
To Smaller	10		
To Larger	9		
TOTAL	19		
Racquet Weight		27	0
To Lighter	12		
To Heavier	2		
TOTAL	14		
Type of Strings		29	1
Nylon to Gut	4		
Gut to Nylon	7		
TOTAL	11		
String Tension		20	8
To Looser	7		
To Tighter	6		
TOTAL	13		

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Congenital Left Ventricular Diverticulum

Part of a Syndrome of Cardiac Anomalies and Midline Defects

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THOMAS L. HUSEBY, M.D.;* and JESSE E. EDWARDS, M.D.*

A case of congenital muscular diverticulum of the left ventricle is presented. This uncommon anomaly, as in the case reported, is usually part of a syndrome characterized by congenital midline thoracic and abdominal defects involving the sternum, diaphragm, anterior abdominal wall, pericardium and heart. Associated cardiac anomalies included ventricular septal defect and asymmetrical hypertrophy of the left ventricle.

A SYNDROME OF congenital cardiac and midline thoracic and abdominal anomalies associated with congenital muscular diverticulum of the left ventricle has been described by Cantrell and associates[1] and others.[2-8,10-13] This syndrome consists of: (1) midline, supraumbilical abdominal wall defect, (2) defect of the lower sternum, (3) deficiency of the anterior diaphragm, (4) defect of the diaphragmatic pericardium and (5) congenital intracardiac defects. In some cases, incomplete expression of the syndrome may occur with one or more of the five defects being absent.

This combination of anomalies has been sometimes described in the literature as the thoracoabdominal type of *ectopia cordis*. However, in 1958, Cantrell and associates[1] suggested that these anomalies constituted a distinct syndrome rather than a type of *ectopia cordis*. True *ectopia cordis* is rarely associated with this group of anomalies; in this syndrome, the heart usually remains in the thorax, its only positional variation being at times a rotational change into the right hemithorax. The "ectopy," more apparent than real, is due to either extrathoracic extension of the ventricular diverticulum or the presence of a midline thoracoabdominal defect which allows visualization of the cardiac impulses.

Report of Case

Clinical Manifestations

A 3,280 gram, full term, male infant was the product of an uncomplicated pregnancy and delivery. Apgar scores were eight at one and five minutes. Physical examination in the delivery room revealed a defect in the rectus abdominus muscle approximately 2 cm. below the region of the xiphoid. In the defect was an expansile, pulsating mass covered by a thin layer of skin (Figure 1). Bilateral, undescended testes and a supernumerary digit of the right hand were also observed.

The infant was transferred to the newborn intensive care unit of the St. Paul Children's Hospital. On arrival, the cardiac and respiratory rates, the temperature and the

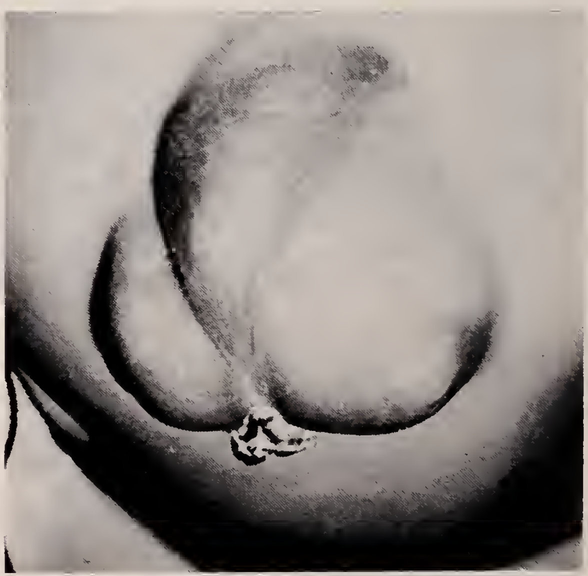

Fig. 1—External view of upper abdomen. Above the umbilicus is a lobulated, pulsatile mass noted at the time of birth.

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flush blood pressure values were within normal limits. Neither cyanosis nor cardiac murmurs were present. An electrocardiogram showed significant intraventricular conduction delay.

A thoracic roentgenogram revealed dextroposition of the heart and normal lungs. The sternum appeared normal. A lateral abdominal film demonstrated that the small pulsatile mass noted clinically was situated in the midline anterior to the liver and in a supine abdominal film, the mass was visible as a midline density projected over the liver and continuous with the cardiac shadow. The mass was felt to represent a ventricular diverticulum because of its location and pulsatile nature.

When five days old, the patient was referred to the University of Minnesota Hospitals where cardiac catheterization and angiocardiography demonstrated an elongated diverticulum arising from the left ventricle, extending below the xiphoid and lying posterior to the anterior abdominal wall defect. The diverticulum contracted vigorously and synchronously with the cardiac beat. An atrial septal defect was noted on the levophase of the examination (Figure 2).

At the age of one month, the patient was readmitted to St. Paul Children's Hospital for elective repair of the midline defects. At operation, a pericardial sac was found to extend into the abdominal cavity through a large anterior diaphragmatic defect (Figure 3) and to contain the left ventricular diverticulum. Several efforts were made to replace the entire heart within the thorax but each attempt caused hypotension and bradycardia. After a trial clamping period, the diverticulum was resected and the heart was placed in the thorax without apparent embarrassment of cardiac function. A silastic graft was used to close the diaphragmatic defect and the superior portion of the identified diastasis recti. The infant was returned to the intensive care unit in satisfactory condition.

On pathologic examination, the resected diverticulum

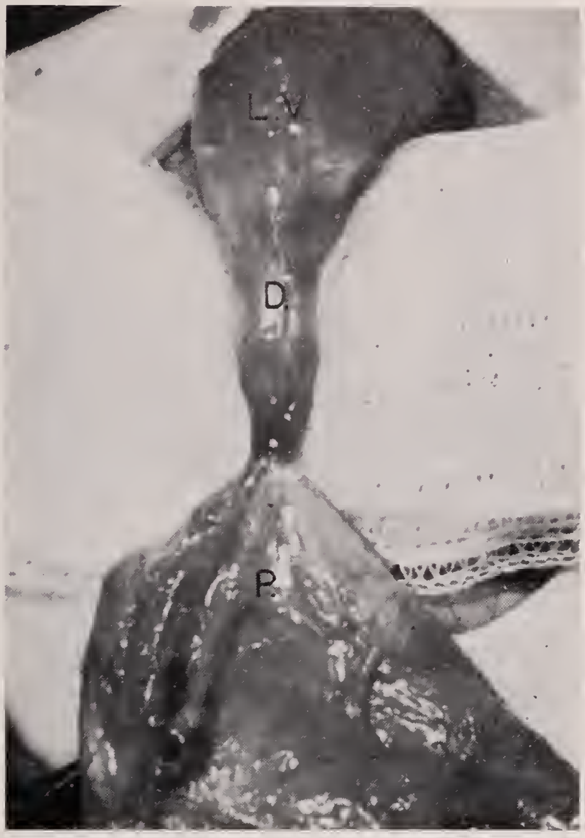

Fig. 3—Surgical exposure of the abdominal portion of the heart. A diverticulum (D.) extends from the left ventricle (L.V.), above; attached to the apex of the exposed diverticulum is the opened and reflected parietal pericardium (P.).

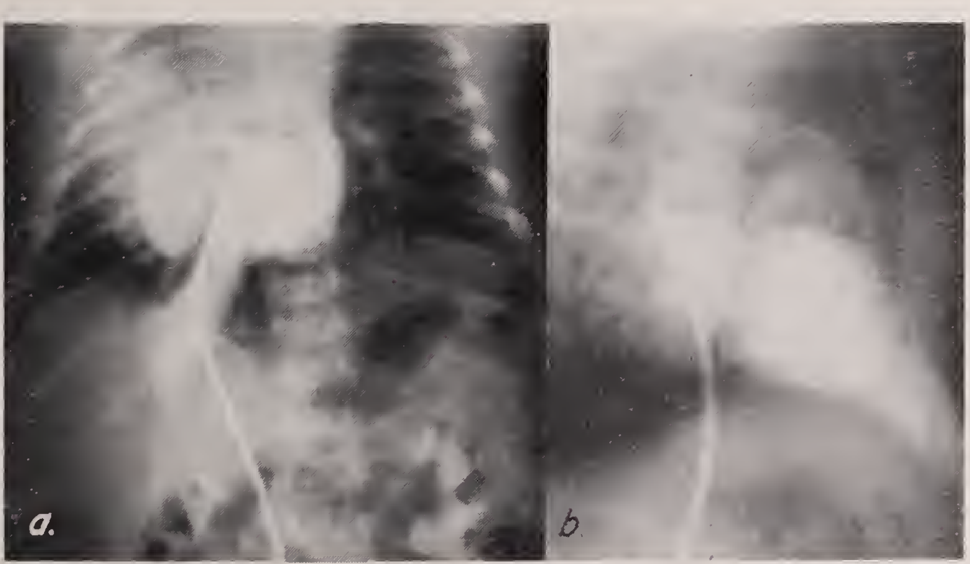

Fig. 2—Left atriogram in frontal (a) and in lateral (b) projections. There is dextroposition of the heart. A discrete diverticulum extends from the apex of the left ventricle into the abdominal region.

was a tubular structure measuring 3 cm. in length and about 1.5 cm in diameter. The narrow cavity was surrounded by a thick wall resembling cardiac muscle. Histologically, the basic structure was similar to that of a cardiac ventricle. A narrow endocardial lined cavity was surrounded by a thick layer of myocardium which was covered by epicardium (Figure 4).

Postoperatively, his course was complicated by intermittent hypotension, seizures and staphylococcal sepsis. Death occurred 48 hours after operation.

At autopsy, additional anomalies of the cardiovascular system consisted of: (1) asymmetrical hypertrophy of the free wall of the base of the left ventricle, (2) a muscular ventricular septal defect, (3) an atrial septal defect at the fossa ovalis and (4) a narrowly patent ductus arteriosus. Except for the anomalies mentioned, the basic structure of each cardiac chamber was normal. The apex of the left ventricle showed evidence of the recent surgery. Suppurative pericarditis was present.

Comment

Our patient represents incomplete expression of the syndrome of congenital midline thoracic and abdominal defects. No sternal defect was demonstrated clinically or radiographically and there was no pericardial defect. The various features of this syndrome will now be briefly discussed.

Midline Abdominal Defect

The midline supraumbilical defect in this case consisted of diastasis recti and a large ventral hernia. Ventral hernia or omphalocele are commonly reported, Toyama noting an omphalocele in more than 60 percent of cases. Diastasis recti of various degrees of severity is the second most common type of expression (30 percent of cases).[12]

The great variability in the expression and degree of severity of defects of the abdominal wall may be explained through consideration of the embryological origin of the abdominal wall. The paired myotomes of each body segment send sheets of migratory muscle cells ventrad toward the midline, completing the process at about seven weeks.

In most of these cases, the rectus muscles are normal but insert more laterally than normal into the costal margins. Therefore, it is believed that the defect is due to a failure of complete ventrad migration of the myotomes.

Midline Sternal Defect

The sternal defect also arises from failure of mesodermal elements, the sclerotomes, to complete their ventrad migration. The lower two-thirds of the sternum are more often involved. Usually there is a midline cleft with sternal bars present on each side. In other cases, the defect may consist of hypoplasia or malformation of the lower sternum or absence of the xiphoid process.

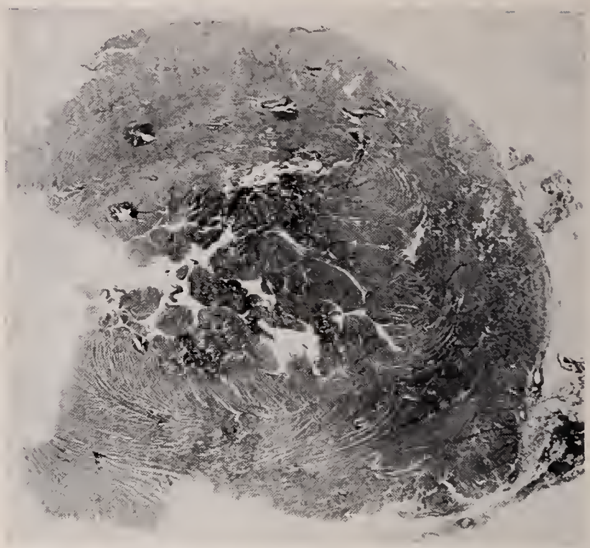

Fig. 4—Photomicrograph of cross section of left ventricular diverticulum removed surgically. The features are similar to those of a cardiac ventricle with endocardium, myocardium and epicardium. (One aspect of the specimen had been incised after removal.) H & E; x 12.5.

Diaphragmatic Defect

The defects of the pericardium and diaphragm in this syndrome are probably related to the lack of development of that ventral shelf or splanchnic mesoderm called the *septum transversum,* since the defect is always found in the area of diaphragm formed by the *septum transversum.* Early in embryologic life the *septum transversum* partially divides the coelomic cavity into thoracic and abdominal portions and gives rise to the ventral portion of the diaphragm. The pleuroperitoneal folds arising from the dorsolateral body walls contribute the dorsal aspect of the diaphragm. This structure is completed by a dorsomedial contribution from the meso-esophagus and lateral contribution from the meso-esophagus and lateral contribution from the body wall.[9]

Pericardial Defect

The cephalic portions of the paired pleuroperitoneal folds are called the pleuropericardial folds. These converge around the heart as the pericardial sac and separate it from the lungs. The caudal aspect of this sac arises from the cephalic aspect of the *septum transversum.*

Because of their common origin, coexisting defects of the diaphragm and inferior aspect of the pericardium are frequently found. However, the patient of Potts and associates had cardiac, abdominal and diaphragmatic anomalies but an intact pericardial sac and sternum[10] and our patient had a large diaphragmatic defect but the pericardial sac was intact.

Cardiac Defects

In cases with the complete expression of this syndrome, a ventricular septal defect has almost invariably been present, quite often as part of the tetralogy of Fallot. Each of the five patients of Cantrell and associates[1] had a ventricular septal defect and Toyama found 27 ventricular septal defects among 37 cases of completely expressed syndromes (approximately 72 percent). Six of these 42 patients had the tetralogy of Fallot. Other associated cardiac anomalies are atrial septal defect, persistent truncus arteriosus, patent ductus arteriosus, tricuspid atresia, diverticulum of the left ventricle and dextroposition of the heart.[12]

A congenital diverticulum of the left ventricle occurs in approximately 20 percent of cases of this syndrome[12] and presents as a pulsatile epigastric mass. The diverticulum extends from the left ventricular cavity. Because it contains normal myocardium in its wall, it contracts normally throughout the cardiac cycle.

According to Parsons,[8] the congenital left ventricular diverticulum may be the result of an abnormal attachment of the cardiac loop to the structures of the yolk sac at about the fourth week of development. As the embryo straightens, the ventricular loop is pulled ventrally, forming a diverticulum anterior to the developing liver. Such an explanation could also account for the midline defects of the sternum and the thoracic and abdominal walls.

Treatment

The commonest cause of death in patients with left ventricular diverticulum is congestive heart failure. Traumatic or spontaneous rupture has also been occasionally reported.[4,14] Because of these potentially life-threatening complications, early surgical correction of a congenital left ventricular diverticulum should be attempted. Cardiac evaluation should be undertaken to evaluate the diverticulum and other intracardiac anomalies with which it is so often associated.

The two methods of treatment for left ventricular diverticulum are either replacement of the intact diverticulum into the pericardial sac intrathoracically or resection of the diverticulum. The latter appears to be the treatment of choice if the diverticulum does not form a significant part of the left ventricular cavity.

If an omphalocele is present, it should be repaired as soon as possible with the simultaneous correction of the diaphragmatic defect.

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Management of Intra-Abdominal Henoch-Schönlein Purpura

The Role of Surgery

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Henoch-Schönlein syndrome may cause abdominal pain. In any patient with a progressive course, the possibility of intussusception and perforation should be considered. The risk of an operation in a patient with intramural intestinal hemorrhage alone is outweighed by the risk in delay of operating on patients with concomitant intestinal intussusception and/or perforation. In cases of Henoch-Schönlein syndrome, hesitation in the decision to operate for suspected intestinal intussusception or perforation may result in a significant increase in mortality.

THE HENOCH-SCHÖNLEIN SYNDROME which occasionally produces abdominal pain can mimic an acute surgical condition. We wish to discuss a case of Henoch-Schönlein purpura with intramural intestinal hemorrhage and infarction that required small bowel resection and treatment with high doses of steroids.

Case Report

In early February 1975 a 5-year-old girl complained of bilateral lower quadrant abdominal pain. A surgeon felt she had possible appendicitis and explored her on February 4, 1975. The abdomen contained too much fluid. Among the findings were: a mildly infected appendix, large mesenteric nodes, and mild erythema and injection of the terminal ileum. He removed the appendix. Three days after surgery, she developed a swollen painful right knee that was aspirated and the culture was sterile. Chest Xray showed bilateral pleural effusion (Figure 1). The knee joint films showed effusion also (Figure 2).

Subsequently she developed mucus and blood in her stool. Red blood cells were found in her urine. She complained of crampy abdominal pain, vomiting several times daily and developing a purpuric rash over the buttocks, pressure points on the heels, feet, and antecubital spaces where tape had been applied. The patient was thought to have an allergic vascular purpura of the Henoch-Schönlein type, and she was referred to Methodist Hospital seven days following appendectomy.

On admission, 2/11/75, the patient weighed 14.5 kg, height 101.6 cm, blood pressure 142/70, pulse 140, and respirations 40-50 per minute. The patient appeared acutely and desperately ill. Skin showed only a slight residual of the purpuric rash on the buttocks. The abdomen was tense and distended, diffusely tender, and had no bowel sounds. There was a large amount of brownish-red liquid stool in the rectal ampulla. Bone and joint examination showed moderate swelling of the right knee.

Laboratory work at the time of admission showed positive stool guaiac. The urine was packed with red

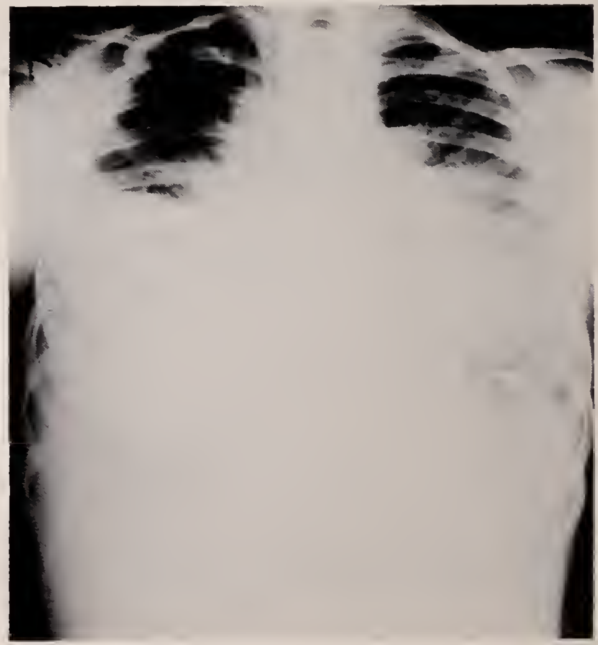

Fig. 1—Chest x-ray film demonstrating bilateral pleural effusion.

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blood cells. Electrolytes were within normal limits. On admission the white blood count was 24,000 with 88% PMNs. Platelet count was 900,000. Abdominal films showed evidence of partial mechanical bowel obstruction with a great deal of peritoneal fluid (Figure 3a). The diagnosis of Henoch-Schönlein purpura or allergic vasculitis was made. The patient was begun on penicillin one million units IV/6hrs, Chloramphenicol 250 mg IV/qid, Surgical consultation was obtained, and it was felt that before the patient could be committed to intensive steroid therapy, the possibility of necrotic bowel disease or intussusception should be excluded.

The patient was taken to surgery on the day of admission, 2/11/75. The abdominal cavity was entered and approximately 300 cc of clear yellowish fluid was present. No pus or other abnormal fluid was found in the abdominal cavity. The small bowel was inspected carefully from the ligament of Treitz to the ileocecal valve. Evidence of severe vasculitis was found throughout the small bowel with hemorrhage of the wall especially in the ileum. Segments of ileum had extensive intramural hemorrhage. A short segment approximately 25 inches from the ileocecal valve, approximately two inches in length, showed gross evidence of impending necrosis. This area of small bowel was resected and an end-to-end anastomosis performed. Histologic examination showed fat necrosis and allergic vasculitis with hemorrhagic necrosis and ulceration of the resected segment of small intestine. These findings were felt to be consistent with a diagnosis of Henoch-Schönlein purpura.

During surgery the patient was given 400 mg hydrocortisone succinate and placed in 200 mgm IV/six hrs, also placed in Chloramphenicol 250 mg IV/six hrs. Postoperatively the patient had a difficult course. She had some premature ventricular contractions which were alleviated by adjustment of her serum electrolytes. The abdomen x-ray films showed some improvement; the small bowel loops were less dilated and the fluid levels were not present (Figure 3b). By the third postoperative day

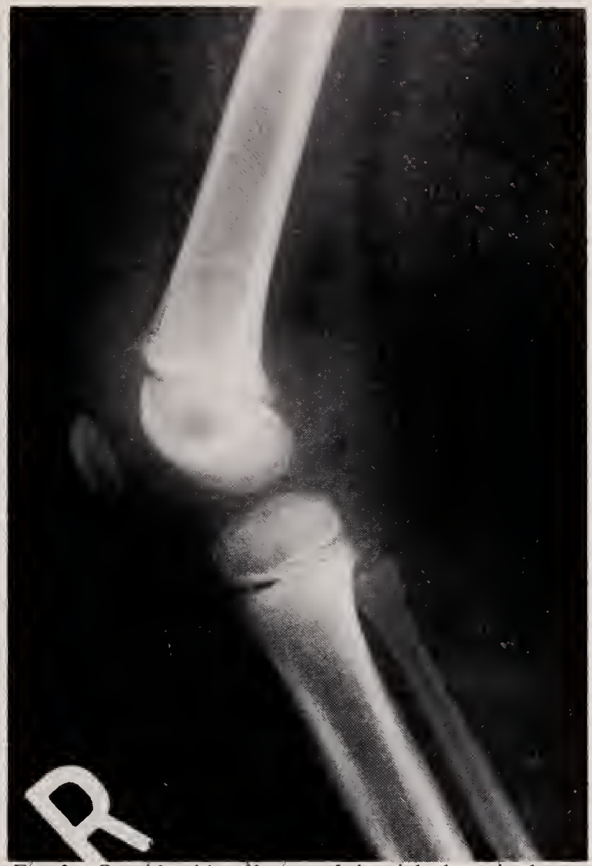

Fig. 2—Considerable effusion of the right knee is shown.

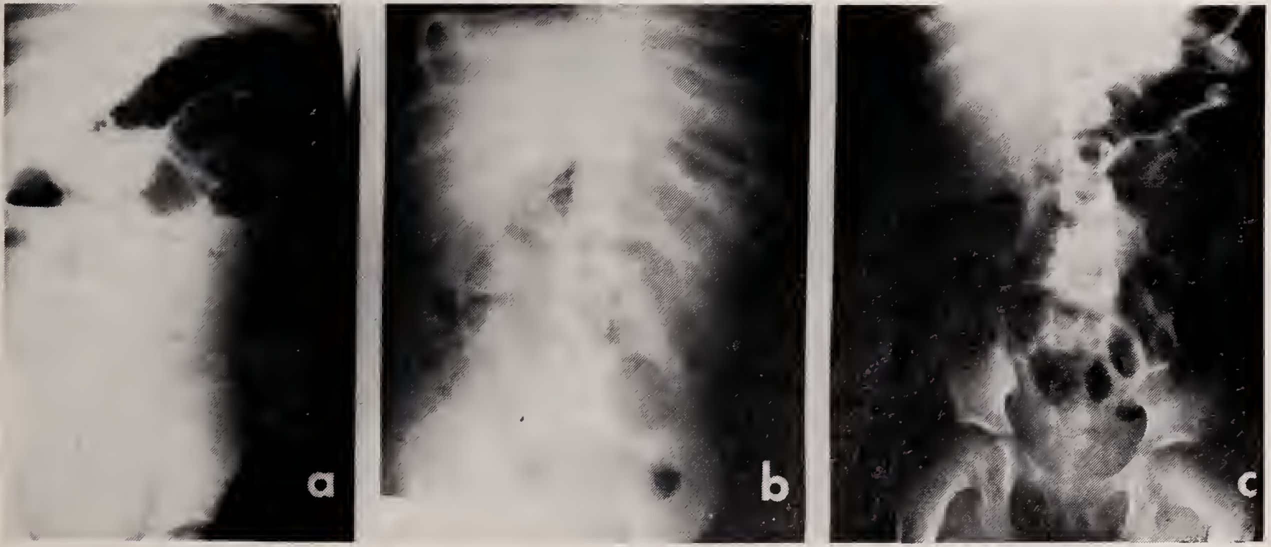

Fig. 3(a)—Fluid levels and significant amount of peritoneal fluid evident which is compatible with small bowel obstruction. (b) Several days after surgery the small bowel loops were moderately dilated and the fluid level images had disappeared. (c) Ten days following surgery the small bowel loops continued being minimally dilated with no image of bowel obstruction.

the patient was expelling flatus and she was placed on oral fluids. On the eighth post-operative day the patient remained afebrile but began to complain of increasing abdominal pain. Abdominal Xrays taken at that time showed possible ileus. Her temperature rose to 102 F and Chloramphenicol, which had been discontinued after the fourth postoperative day, was again started at 250 mg IV/6 hrs. Her white blood count was 32,000. Examination of the abdomen revealed extreme tenderness and slight distention. Bowel sounds were active. Roentgenograms subsequently showed more distention in the small bowel suggestive of paralytic ileus. The following day the patient improved and became afebrile with less abdominal pain and tenderness. The steroid dose was decreased, and the patient continued to improve steadily, expelling flatus and having bowel movements. The steroids were decreased to 100 mg hydrocortisone succinate/8 hrs. Urinalysis obtained at various intervals during the patient's postoperative course had shown occasional RBCs and the stools continued to be guaiac positive. The abdomen X-ray films showed minimal distention of small bowel loops with intramural edema (Figure 3c). Additional potassium was given to supplement the urinary losses. The patient continued a gradual improvement. Her antibiotics were discontinued on the 14th hospital day. She was placed on oral prednisone in gradual decreasing amounts and was receiving five mg/bid at the time of discharge, her 24th hospital day (Figure 4).

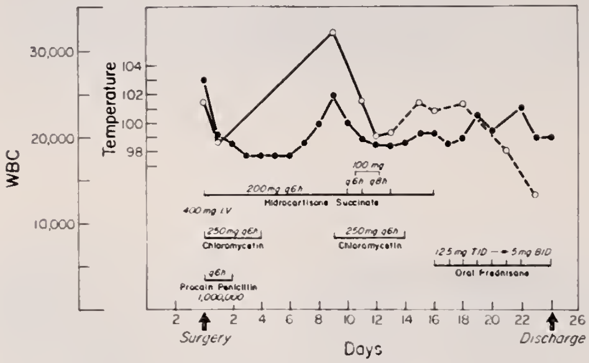

Fig. 4—A sharp decrease of temperature and white blood cells immediately after surgery was followed by a continuous gradual increase up to the eighth postoperative day with a subsequent decrease when the Chloromycetin was added. Thereafter, the postoperative course was steady until discharge.

Ten days later, during which time steroids had been discontinued, she was readmitted with fever and right lower quadrant pain. Physical examination revealed a pale female in moderate acute distress. Her temperature was 101 F orally. Physical examination was unremarkable except for some guarding on the right side with questionable rebound. Laboratory data showed Hgb 11.2 gms%, WBC 9,000, urinalysis showed some microscopic hematuria, and her stool guaiac was positive. Xray showed a small air-fluid collection in the right upper quadrant. The possibility of a small abscess cavity was raised.

The patient was replaced on 10 mg prednisone/bid as well as penicillin and Chloromycetin. Her temperature returned to normal within 12 hours and her right-sided pain rapidly resolved. Antibiotics were discontinued four days later, and she was discharged on the sixth hospital day on prednisone 5 mg/bid.

Discussion

Medical management of the Henoch-Schönlein syndrome with steroids remains the preferred approach. Surgical intervention remains controversial particularly in the absence of peritonitis. This syndrome may cause acute abdominal pain and, when there is no rash, the diagnosis may not be apparent. The onset of abdominal pain preceding the rash is not uncommon and may result in unnecessary surgical intervention.

Is there a role for surgery in the total management of this disease? The risk of an operation in a patient with purpura is increased due to bleeding and increased incidence of wound infection.[4] In addition, these patients are placed on high doses of steroids which may delay wound healing. However, intussusception or perforation requires prompt surgical intervention. In abdominal purpura it is often difficult to rule out the co-existence of intussusception, obstruction, or perforation. Fortunately, intussusception and perforation are rare. A review of the world literature[5-11] reported 6% of intussusception in approximately 60 cases of Henoch-Schönlein syndrome. In addition, 12 cases of perforation associated with this disease have been reported.[12-19]

Surgical procedures in Henoch-Schönlein syndrome have always been approached with trepidation. In 1918, Bailey[20] reviewed 30 cases of abdominal purpura in which 14 patients had intussusception and 16 had intramural hemorrhage. Of those with intussusception, nine were operated on with one death (11%); five were not, with three deaths (60%). Of the 16 without intussusception who were operated on, five died (31%).[20] Steinhardt and Jonas[4] in 1957 studied 26 cases with intussusception. Twenty patients (76%) were operated on, 55% underwent resections, and the remaining 45% were easily reducible. The large number of resections reflects delay in reaching the decision to operate. The mortality in the patients operated on was 20%. All postsurgical deaths, except where intussusception recurred, occurred in those that underwent resection. Of the six patients who had no operation, three patients died.[4] It is evident from these studies that the risk inherent in operating upon patients with abdominal purpura is far outweighed by the risk in delaying operating in individuals with intestinal intussusception or perforation. The large number of resections would suggest that delay in deciding to operate resulted in the need for more extensive procedures, whereas a less extensive surgical procedure would have been required if performed at an earlier time.

Although no specific findings are diagnostic of an associated intussusception or perforation, some clinical and laboratory signs may be valuable in identifying patients needing surgery. A high persistent fever, marked leukocytosis with shift toward the left, and peritoneal signs as rigidity and rebound rarely occur in the uncomplicated case. Plain films of the abdomen may be helpful in revealing obstruction or the presence of free air in abdomen. A peritoneal tap may be helpful. Barium enema may reveal the site of obstruction. In general, any patient who had a sudden increase of his abdominal pain or a persistent pain should be considered a surgical candidate.

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Association of Neurologists of Minnesota

The Association of Neurologists of Minnesota was formed to deal with economic and legal problems facing neurologists in practice. Donald W. Mulder, M.D., is President, and Andrew J. Leemhuis, M.D., is Vice President. Communications may be addressed to the Secretary-Treasurer, Robert J. Gumnit, M.D., at his office at 640 Jackson Street, St. Paul, Minnesota 55101.

Owen H. Wangensteen, M.D.

Dr. Owen Wangensteen was the recipient of the Distinguished Scientific Achievement Award presented to him by the Council of the American Surgical Association at its meeting in New Orleans in April.

"Silent Thyroiditis" Versus Thyrotoxicosis Factitia

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A patient is discussed who presented with thyrotoxicosis associated with a markedly depressed fractional and 24-hour thyroidal uptake of I-131. The patient's socio-economic status suggested factitious use of thyroid hormone. The lack of goiter, thyroid pain, and elevated erythrocyte sedimentation rates were features against a diagnosis of subacute thyroiditis. The patient's illness is similar to previously described cases of "silent thyroiditis." The controversy exists as to whether this form of thyrotoxicosis is due to atypical subacute thyroiditis or a newly described variant of lymphocytic thyroiditis. In our case, this conflict was resolved by thyroid biopsy which showed the extensive infiltrative and destructive process of lymphocytic thyroiditis. This form of lymphocytic thyroiditis is distinctly different from Hashitoxicosis. The clinical course of previously described patients with "silent thyroiditis" has been one associated with frequent development of hypothyroidism.

THE OCCURRENCE OF hyperthyroidism in association with a suppressed thyroidal radioiodine uptake leads one to consider such disease processes as subacute thyroiditis, lymphocytic thyroiditis, ectopic thyroid hormone production (e.g. struma ovarii) or thyrotoxicosis factitia. Papapetrou and Jackson have[1] recently reported "silent thyroiditis" as a cause of thyrotoxicosis. They presumed that their patient's disease was caused by subacute thyroiditis although this diagnosis is questionable by the findings of Plymate and Nusynowitz.[2-4] Although the clinical course and presentation of their patients is consistent with previously described cases of painless (atypical) subacute thyroiditis,[5-8] thyroid biopsy may have shown lymphocytic thyroiditis.[2-4] Our patient was initially considered to represent factitious thyrotoxicosis, however, biopsy of his thyroid gland revealed lymphocytic thyroiditis. This case further defines the spectrum of atypical forms of hyperthyroidism and emphasizes the importance of biopsy to establish diagnosis and predict subsequent prognosis in atypical cases.

Case Report

The patient, a 32-year-old married Air Force Captain, was referred to Fitzsimons Army Medical Center for evaluation of hyperthyroidism. He related a two-month history of increasing insomnia, nervousness, "hot flashes" and tachycardia. There were no changes in bowel habits, heat intolerance, or any significant weight loss. He specifically denied any history of sore throat, thyroid pain or ever having taken thyroid or other medication. Recently he had been selected for military reduction in force (RIF) much to his dissatisfaction. While undergoing processing for separation, he was concerned regarding medical disability for his thyroid condition. His wife is a licensed practical nurse and is enrolled in a registered nurses training program. His previous workup included a resin T4 that was 17.3 ug/100 ml (upper normal $<$ 11.5 ug/100 ml), resin T3 of 51.5% (upper normal $<$ 45%), free thyroxine index of 9 (upper normal $<$ 5). An RAI uptake was 0% at 6 and 24 hours on one occasion and 1 and 0% at 6 and 24 hours respectively on a second occasion. The patient was placed on Propranolol, 20 mg q.i.d., for control of sinus tachycardia. He was transferred to Fitzsimons for evaluation of probable thyroiditis. His past medical history and family history are non-contributory. His social history is positive in the fact that he was notified one month prior to onset of symptoms that he was going to undergo the RIF.

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The opinions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or Department of Defense.

Physical examination revealed a well developed, well nourished white male in no acute distress. Height of 178 cm. body weight of 79.15 kilograms, body temperature 36.6 degrees centigrade, pulse regular with a rate of 74; blood pressure supine was 118/70. General physical exam was unremarkable except for warm, moist skin. Examination of his neck revealed a symmetrical, nontender thyroid, approximately 20 grams in size and of normal consistency with no nodularity. Clinical impression was hyperthyroidism, probably secondary to thyroiditis but self administration of thyroid hormone was considered.

The patient's laboratory findings are presented in the Table. These results demonstrate evidence of thyroid hormone excess in the presence of a suppressed fractional and 24 hour thyroidal I-131 uptake. The PBI-T4 discrepancy is accounted for by discharge of iodine, and/or iodinated products from the thyroid gland. Serial ESR measurements were normal. The thyroid hemagglutinating antibody titer and microsomal antibody titers were negative. Whole body scanning for ectopic thyroid tissue was negative. Noteworthy was normal erythrocyte sedimentation rates (ESR) on five occasions. In view of the repeated normal ETR and white blood counts, the question was posed to patient again of the possibility of ingestion of thyroid hormone. He again denied any ingestion of thyroid medication. He underwent a thyroid biopsy of both the right and left lobes. Pathology findings were consistent with lymphocytic thyroiditis showing extensive destruction of thyroid follicles by lymphocytic infiltrate with follicle formation (Figures 1 and 2) and the presence of Askanazy cells. The patient has continued under symptomatic therapy for his hyperthyroidism with propanolol and phenobarbital.

Discussion

Thyrotoxicosis factitia was initially considered

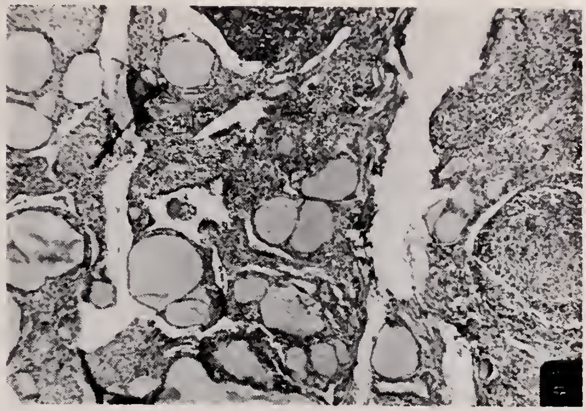

Fig. 1—Diffuse lymphocytic infiltration throughout thyroid parenchyma and isolated areas of lymphoid follicle formation are demonstrated.

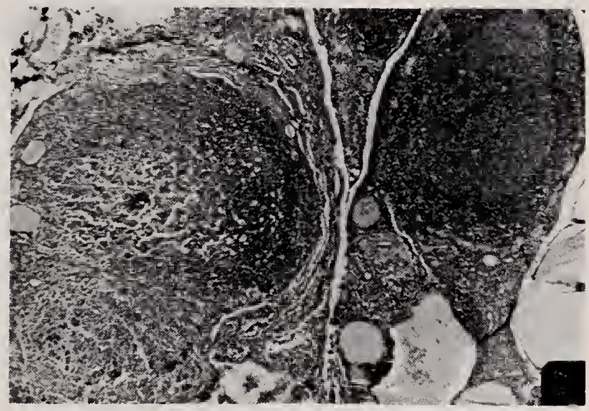

Fig. 2—Multiple areas of lymphoid follicle formation with germinal centers are shown throughout thyroid parenchyma and thyroid tissue is severely infiltrated by this inflammatory process.

TABLE
Laboratory Values

	Patients' Values	Normal Values
I^{131} Uptake		
4 hours	1.0%	3-14%
24 hours	0.5%	8-30%
PBI	12 μg%	4-8 μg%
Column T_4	6.2 μg%	2.8-6.4 μg%
Resin T_3 uptake	41%	25-35%
Thyroid index*	2.5	0.8-2.2
TSH	1.0 μU/ml	$<$6.5 μU/ml
Thyroid antimicrosomal antibodies†		
by immunofluorescent staining	nondetectable	nondetectable
by complement fixation	$<$4	$<$4
Thyroglobulin microtiter by HA (Wellxome)‡	1:160	$<$2,500
Thyroglobulin microtiter by HA (Ames)‡	$<$1:100	$<$1:1,600
Antimicrosomal microtiter by HA (Ames)‡	1:100	$<$1:1,600
Sedimentation rates (mm/hr)		
April 18	6	0-12
21	6	
22	6	
23	7	
24	6	
27	6	

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*Multiplication product of Resin T_3 uptake X Column T_4 to give an adjusted thyroid index
†Bio-Science Laboratories (7600 Tyrone Avenue, Van Nuys, California 91405)
‡Sixth Army Area Laboratory (Ft. Baker, California 94965)

in this patient because of the availability and access to thyroid hormone from his nurse-wife, perhaps related to a behavioral disturbance caused by his pending military RIF. Repeated examinations of his thyroid gland demonstrated a normal-sized, nontender gland. His thyroid I-131 uptake was markedly suppressed and whole body scanning procedures showed no evidence of ectopic thyroid tissue. The patient's ESR was normal, making the diagnosis of subacute thyroiditis unlikely.[7,9] Thyroid biopsy showed the characteristic histological features of lymphocytic thyroiditis.

Iodide administration can suppress the 24-hour uptake and can induce an iodide form of hyperthyroidism (Jadbasedow phenomenon); however, when these patients are evaluated during their thyrotoxic state, the thyroidal uptakes are not suppressed,[10] and this condition has not previously been reported with suppressed uptakes.[10-11]

Similarly, patients with Graves disease who ingest large quantities of iodide-containing compounds might present with elevated serum thyroid hormone measurements and a depressed thyroidal RAI uptake. Such iodide blockade of the RAI uptake in these patients is short-lived with values returning to the hyperthyroid ranges within three weeks or less.[6] Likewise, nonthyrotoxic patients given iodides may present with a high PBI and suppressed thyroidal RAI uptake; however, the infrequent use of the PBI today and the more common laboratory specific thyroxine measurement avoids this confusion.

Of the various forms of atypical thyrotoxicosis associated with a suppressed thyroid uptake, "silent thyroiditis" has been the most recently reported variant. The three initial cases were considered a manifestation of subacute thyroiditis occurring in individuals with nontender thyroid glands.[1] Noteworthy was that one of these patients subsequently developed hypothyroidism which is unusual in subacute thyroiditis.[7,9] In their patients, the ESR was not reported and anti-thyroid antibody titers when measured were low. In a larger series of patients reported by Plymate and Nusynowitz,[2-4] there were similar features of hyperthyroidism, nontender thyroid glands, normal ESR and suppressed thyroidal uptakes. Biopsies of these glands showed lymphocytic thyroiditis. Subsequent course after resolution of the hyperthyroid state was one of euthyroidism or hypothyroidism.

We would suggest that these earlier described cases of "silent thyroiditis"[1] reported as variants of subacute thyroiditis were actually lymphocytic thyroiditis. This unusual form of lymphocytic thyroiditis masquerades as subacute thyroiditis but in reality it represents a newly defined variant of thyrotoxicosis associated with Hashimoto's thyroiditis and is distinctly different from Hashitoxicosis. Patients with Hashitoxicosis present with hyperthyroidism, normal to elevated, nonsuppressible radioactive thyroidal I-131 uptakes, and high thyroglobulin antibody titers.[12-14] A high incidence of hypothyroidism follows subtotal thyroidectomy or I-131 treatment in these patients.

Histological examination of goiterous tissue in Grave's disease frequently shows evidence of lymphocytic infiltration. An extensive lymphocytic infiltration is characteristically seen within the Hashimoto's thyroid gland. "Silent thyroiditis" due to this lymphocytic process has features of both subacute thyroiditis and Hashitoxicosis. The clinical presentation is consistent with an active inflammatory process with impairment of thyroid cell function which is associated with the discharge of thyroid hormone and iodinated products which further account for the low thyroid uptake and thyrotoxic state. The occurrence of this disease in older individuals, frequently males, (two or three of Papapetrou's cases) with asymptomatic normal-sized thyroid glands, normal ESR and subsequent occurrence of hypothyroidism appear to be its distinguishing features. The disease must be distinguished from factitious thyrotoxicosis. Likewise, the disease has distinctly different characteristics from Hashitoxicosis, although both forms appear to have a high associaton with the development of subsequent hypothyroidism.

Since thyrotoxic patients may display personality and emotional behavioral disorders[15] and on occasion criminal behavior,[16] thyrotoxicosis factitia is always a consideration when evaluating patients with this type of presentation. Surgical biopsy of the thyroid gland will establish the presence of lymphocytic thyroiditis and allows a clear distinction between "occult subacute thyroiditis" (De Quervain's),[5,8] lymphocytic thyroiditis,[2-4] sarcoidosis[17] and factitious disease.[18]

Acknowledgments

The authors wish to acknowledge Ms. Deborah Longbofer, Renee' Pierce and Laurie Renner for secretarial and editing assistance in the preparation on the text: laboratory technicians Karen Preston, John Pesut, and Anne Dolbow; and Mr. William R. Hommel of Medical Illustrations.

References will be found on page 429.

An Interview with Richard E. Anonsen, M.D.

President, Minnesota State Medical Association

One of the purposes of MINNESOTA MEDICINE is to convey messages from Association leaders to members. For some reason, this has been an awkward process. Usually the messages have taken the form of stiffly worded memoranda, editorials, announcements, or even as recorded minutes. Once a month, the President's Letter appears in the journal. But this letter traditionally occupies only one page, and the President has little room to present more than one idea at a time. The thought occurred that an interview might be a comfortable format for the President or other Association leaders to present a wider range of their personal views.

The interview took place in Doctor Anonsen's paneled office at the Tyrol Clinic, a one story white brick building just off Wayzata Boulevard. The office contains memorabilia from Doctor Anonsen's football days at the University of Minnesota from 1948 to 1950. Also a silver bowl, awarded to him in appreciation from the Foundation of Health Care sits on a table. And on his desk there is a small statue called The Sprites. Metropolitan Medical Center awarded him the statue for his outstanding community service, especially his role in forming the Hennepin County Medical Foundation. The interview took about 45 minutes to complete. Doctor Farrell Stiegler took the pictures.

Richard C. Reece, M.D.
Editor-in-Chief

Interviewer: *As the new President of the Minnesota State Medical Association, what do you want to accomplish?*
Anonsen:

The major thing, I think, is to set up the Division of Socioeconomic Affairs so it can begin functioning immediately. This Division, under its Director, Jim Rosevear, will deal with the whole range of medical socio-economic problems facing physicians in Minnesota.

Interviewer: *What are the major legislative problems?*
Anonsen:

Malpractice and its ramifications. We have proposed several bills to the legislature. But we're not in the position California is in. We are able to obtain malpractice insurance. We also have a statute of limitations of two years. This is better than any place in the country.

In other words, we feel we have time. We can learn by watching other states such as Indiana and Michigan where they have enacted comprehensive packages of legislature relating to professional liability. We can also evaluate our own program of voluntary binding arbitration.

Interviewer: *What do you think about the catastrophic health bill just passed in the Minnesota legislature?*

Anonsen:

What disturbs me about the bill are these matters: Who will determine what a catastrophic illness is; what diagnoses are involved; and who will do the peer review and monitoring? We are presuming that physicians will participate in the review process. Medicine—not government—should decide what is catastrophic.

Interviewer: *Would you say a patient with crippling rheumatoid arthritis has a catastrophic illness? Arthritis may not threaten life, but it empties the pocketbook.*

Anonsen:

I would go with the judgment of the physician who knows and has examined the patient.

But I'm frightened who is going to decide who gets expensive, or prolonged, or catastrophic, or hard to get care.

Who is going to have a coronary bypass, or an organ transplant, or renal dialysis?

Is an anonymous review board going to decide when I'm 65 and retired on a fixed income that I can't have the same operations others will have in the working income-producing age groups? Is Medicine headed towards a quantitation of services based on price, rather than on quality based on medical indications?

Doctor Walter McClure makes this point in all his speeches: America cannot afford quality medical care for everybody. Therefore, somebody, maybe a review organization, has to decide who can have the more sophisticated and expensive procedures to return that person to society. That idea frightens me.

Interviewer: *But that's precisely what a review committee is doing in the State of Washington now with kidney transplants. A citizens' committee decides who gets the kidney. Let's return to the catastrophic health bill. Are you saying the legislature doesn't specifically spell out who is on the review board?*

Anonsen:

Not yet. However, as a result of a Minnesota State Medical Association amendment the determination of medical necessity shall be the responsibility of a review organization such as the Foundation for Health Care Evaluation.

Interviewer: *May I jump from the State Legislature to Congress? What is the status of PSRO legislation, and what is the Association's attitude toward PSRO?*

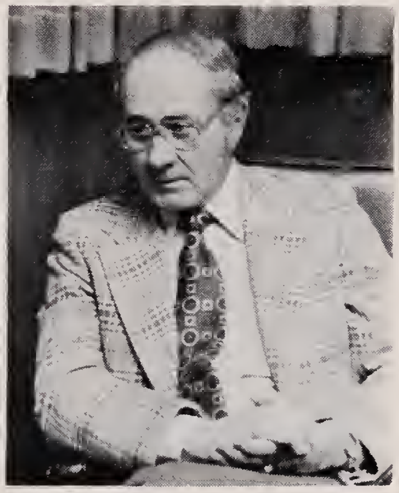
Anonsen:

First, we have just received word that the PSRO for northern Minnesota has been amalgamated with the PSRO of the Metropolitan area. That is the best thing that could have happened. We are now down to two PSROs for the state. The important thing here is that we now escape the Governor's advisory committee. Instead a Board of Physicians and Consumers will run the PSRO.

PSRO legislation is having a difficult time getting funding. We don't know how long the federal government will continue to fund PSROs.

But we do know our Foundation is working. It is working because it came from the grass roots. It came voluntarily because physicians planned, organized, and operated it.

PSROs now bring in millions of dollars for length of stay or utilization review, for quality assurance review, and for admission certification. We had difficulty accepting admission certification review as demanded by PSRO legislation in 24-48 hours. The AMA obtained an injunction and now the regulations have been rewritten to allow this review to be performed in 72 hours which time-wise is more feasible.



Interviewer: *PSROs were to take effect in January 1976 but were postponed. Do you have any idea when PSROs will become official, if at all?*

Anonsen:

It will depend on money. Will the federal government be willing to spend millions of dollars to support 202 PSROs? Is it going to be worthwhile, for example, to spend half a billion dollars to reduce the hospital stay from 7.8 days to 7.6 days?

When PSROs take hold, we're going to find out "quality medicine," as defined by the government, will be extremely expensive. My efforts are now directed toward obtaining changes in the PSRO law. The intent of the law as passed by Congress has been changed as it has been implemented by HEW. The AMA has submitted nineteen amendments to the existing law to Congress, has successfully obtained passage of three of them including postponing the authority for the secretary of HEW to enter into PSRO contracts with groups other than professional associations until July 1, 1978. The sixteen amendments remaining include such vital issues as confidentiality of data (we are opposed to using social security numbers for identifying providers or patients) and guidelines (referring to norms, criteria, and standards) are to be guides only and cannot be substantiated for individual professional judgment with local authority and variations in developing these guidelines.

Interviewer: *What do you think the prospects are for National Health Insurance this year?*
Anonsen:

They'll be excellent after the election. There are now approximately 19 bills before Congress. The federal government cannot presently afford a Kennedy type plan. So Congress will probably begin with catastrophic insurance, just the Minnesota legislature did, then work towards a total system.

Interviewer: *Has the recession stalled a National Health Bill?*
Anonsen:

Certainly. With the recession, everyone is asking: How much is it going to cost? One hundred and twenty billion dollars? Well, we can't afford it.

Medicare and Medicaid cost 100 percent more than statisticians forecast, even though the AMA warned them.

In Hennepin County, prior to 1966, 11 percent of those over 65 were hospitalized each year. After Medicare and Medicaid became law, the percent doubled—to 23 percent. This increase was not due to more sick people getting treated. Look at HMOs, who concentrates on well people. Marshfield Clinic in Wisconsin found that people with the same diagnosis were seen 25% more by the physician if they were under the HMO prepayment plan than a fee for service plan.

Under HMO plans, the worried well are going to crowd our offices, but the very ill are going to have a difficult time getting into the system.

Interviewer: *So, in effect, HMOs will increase demand and therefore increase costs?*
Anonsen: That's right.

Interviewer: *How do you feel about the Hennepin County open wall HMO?*
Anonsen:

The physicians of Hennepin County are attempting to deliver medical care with a choice to their patients. The physicians are giving the patients a choice: fee-for-service or HMO?

As with the Hennepin County Foundation, the physicians have taken the initiative. With the Foundation, the physicians themselves set up a peer review mechanism to improve the quality of medical care. Now the physicians are giving a freedom of choice between alternative types of health care delivery.

My deepest concern with HMO's behavior is present action by Congress on S 1926 "Health Maintenance Organization Amendments of 1975." Basically this law seeks a substantial reduction in what are now considered to be basic health services provided under the HMO law. It is true that this reduction would result in lower costs for HMO operation and this would seem to be an admirable objective. However, there is another side to this two-edged sword. The important point here is that while the reduction of these services should have a cost saving benefit, the HMO is no longer in a competitive position—if it ever really was—with other physician health care provider group systems.

If the intent is to prove that an HMO is less costly than physician health care outside the HMO framework, then the reduction of these essential services will probably work in proving that point.

Many of the provisions in these amendments are designed to create a more attractive environment for the HMO. For example, the elimination of "open enrollment" creates a situation where an HMO is protected against having to accept patients who are likely to demand many services because of their health.

To remove coverage of dental care for children, care of chemical dependency, care of mental illness, etc., from the basic coverage in HMO insurance plans brings a disservice to members enrolled in such HMOs and provides those HMOs with a competitive edge over other forms of medical practice which are providing full services.

Interviewer: *Then economics is really the name of the game. When Doctor Richard Egdahl was here a couple of years ago, he spoke to the Foundation and said doctors have to take some of the risk in the finances of Medicine because the doctors control most of the health care dollar. How can doctors take some of the risk?*

Anonsen:

Well, we are taking the risk in this open wall HMO by allowing 20% of our fees to be placed in a contingency fund. The patients are guaranteed total care for a fixed price, and we have guaranteed them in return that we will care for them for 12 months under this contract. If expenses exceed the fixed price, physicians will lose the 20 percent or more.

Interviewer: *Dr. Anonsen, you were instrumental in forming the Hennepin County Foundation. How has this worked and do you think it has anything applicable statewide?*

Anonsen:

The Foundation for Health Care Evaluation started in Hennepin County and then spread to the seven county area. As you know, the Foundation is instrumental in primary peer review, quality utilization, and admission certification in hospitals. Three years ago under the action of the House of Delegates, the Foundation became a statewide organization.

Interviewer: *Is there any way you can advise Minnesota physicians to participate more actively in the State Association so we can be more of a collective force?*

Anonsen:

Yes. First, get to know your state legislators, and advise them by supplying the legislator with information. Make them aware of our problems and our suggestions for solutions. Secondly, participate directly in the county medical society to become better informed. Third, attend the State meetings.

Interviewer: *How do you plan to improve the image of the medical profession to the public? Do you see any ways the Association can act to present our positive accomplishments?*

Anonsen:

This is an area that we need improvement. We have a positive story to tell. I'm proud to be a physician, and I'm proud of the medical profession, but we haven't been able to relate our positive points to the public. People say "I like my doctor but all other doctors are bad."

Now that means that we aren't doing our job and I think that the state association should start a public relations department to tell our story not only the socio-economic aspects of our practices but the positive points of the type of medicine that we're delivering to the public.

Whether it's in an ambulatory setting, hospital setting, research setting, there are medical stories and economic stories that we should be telling that we aren't. The people are not informed of this aspect.

They get the negative aspect from the national media; they hear about the problems caused by sick doctors or unethical doctors but not the other side. And in this area of ethics or the sick physician, we're trying to take positive points by having them before what we now call the sick doctor committee, the ethical committee both of the county and state societies and, hopefully, by policing our own people we can erase the negative aspect and by creating a new department of public relations we can sell the positive points to the people of the State of Minnesota. I feel we should have a public relations director who has experience in writing and speaking and start telling our story.

Interviewer: *But how do you identify and single out the sick physician?*

Anonsen:

His colleagues have to identify him.

Interviewer: *How do you get your colleagues to do that?*

Anonsen:

It's difficult. You have to identify the problem physician in the hospital where you're practicing with him. You have to bring his problem to the attention of your colleagues, and you have to refer him to the Sick Doctors Committee of the County Society.

Interviewer: *The mechanism exists, but the motivating force isn't there. We may have seen physicians who are unethical or incompetent or sick, but we hesitate to act against them.*

Anonsen:

We have to begin taking action. Perhaps we can motivate physi-

cians to inform fellow physicians by giving the observer or accuser immunity from the legal process. In any event, the evidence is going to have to be well-documented, and we will have to go through a judicial process to remove the physician from practice in the institution.

Interviewer: *We have discussed many problems. Do you see prospects for accomplishment this year—for contributing something that will better the status of Minnesota physicians?*
Anonsen:

Yes, I think if we can develop a department of public relations with an effective head; if we can have a strong division of socioeconomic affairs, and if both these units will get out to the people, get out to the physicians, and inform them and encourage and obtain their cooperation instead of the apathy that is present now, I think that the year will be magnificent.

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University of Minnesota

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* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

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Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

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Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

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Usage in Children: Clinical studies establishing safety and effectiveness in child
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Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blur
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Editorials

Michigan Alcoholic Screening Test

DR. BREITENBUCHER'S* basic beliefs regarding alcoholism are in my opinion correct. It is certainly well known in the field of alcoholism that the medical centers of higher learning are indifferent to the problem, and naturally and consequently the students learn to be indifferent. Of course it is not so much a matter of incompetence on the part of the teachers of medical students as much as it is a misconception about the nature of the problem and who has it. Their teachers had no education about it either.

Even though the MAST Test seems conservative in screening out those with drinking problems it really isn't. In my opinion the positive responses as scored by the test detect very serious middle or late stage alcoholism. My only negative criticism of the test is that it does not differentiate alcohol addicts from serious chronic alcohol abusers (Heavy "Social" drinkers). It is being found that the latter category is in almost as much difficulty as the alcoholic addicts, especially in physical complications they suffer and difficulty in stopping drinking.

Further evaluation after detection of a drinking problem by the MAST Test would differentiate this latter category and a different approach to "treatment" would probably be indicated. This is because the heavy "social" abuser could not identify or accept justifiably an alcohol addiction label.

I have recently been quite impressed with the increased sensitivity of physicians to the alcoholic problem and their receptivity to suggestions of how to diagnose and deal with it. I feel this paper will have very significant impact on physicians who read it.

Richard O. Heilman, M.D.†
Minneapolis, Minnesota

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*See page 425.

†Director, Drug Dependency Treatment Program, Veterans Hospital, Minneapolis, Minnesota.

Erosion of Indian Mental Health in Cities

DR. WESTERMEYER* has attempted to make understandable the "erosion of Indian mental health" by briefly describing the crucial problems Indians face in our society and in turn the problems non-Indian majority face in understanding Indians. Other authors have described the merits of an Indian Nation within the majority society or nation.

As this article implies, problems remain even if Indians and whites mix. Further moves made to cooperate might bridge the obvious gap between these two peoples. Well-meaning non-Indians remain relatively impotent to help significantly other than in "bandaid" fashion.

Maybe Indians themselves will question whether they can afford cultural identity and separation despite the obvious desire to avoid modeling themselves after the majority model. Perhaps

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*See page 431.

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Complete literature available on request from Professional Services Dept. PML.

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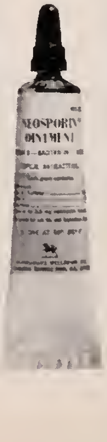

"compromise" with the majority model is necessary to a greater degree for cultural identity to have meaning let alone survival value. The reservation and its dependency enhancing and destroying characteristics can be tolerated by Indians much longer. It tends to provide an enticing haven which is but a shadow of what once was a workable, valuable socioeconomic system but which now located in isolated, fragmented small areas within a majority and alien socioeconomic system is only shadow and illusory of any real security and nurturence.

For Indians to fare well off the reservation some Indians must participate in the majority society to become care givers to their own people. Likewise for the reservation to more than exist some Indians must successfully bridge the gap between the two systems and establish the "currency exchange" to allow the two socioeconomic systems to function next to each other. Short of this Indians must necessarily become part of the majority and wistfully hold on to their culture as the Europeans, Africans, Mexicans, Polynesians, and Orientals in our society have been forced to do. For many reasons we must work with Indian people to determine with them what systems serve them best over time. Articles such as this help us to appreciate the complexity of these problems.

James D. Swenson, M.D.
Minneapolis, Minnesota

Twenty-Five Years Association of a Psychiatrist

For a psychiatrist to be an active member of, and listed on the faculty roster of, the Department of Obstetrics and Gynecology may seem unusual.

This first occurred at the University of Minnesota in 1951. This article states that the request for such an appointment was made by the psychiatrist and soon after was granted.

Dr. McKelvey had this plan in mind and welcomed the appearance of a psychiatrist with this desire. These intervening twenty-five years have demonstrated the wisdom of the decision. The benefits to the patients firstly, and to the staff and medical students secondly have been the rewards.

This presentation was made before the Central Travel Club in September 1975 in Minneapolis. This group of men, all active in our specialty, were duly impressed. The idea was new to many of them. They expressed a desire to implement the plan in their home areas. Nearly all of the guests are active in the academic endeavors in their respective cities.

John A. Haugen, M.D.
Minneapolis, Minnesota

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*Minnesota Med 59:341, 1976.

Cover Painting

"Old Fort at Grand Portage"

The Editors of MINNESOTA MEDICINE commissioned Dr. Tague Chisholm, a well-known Minneapolis pediatric surgeon, to paint the cover watercolor in honor of the Bicentennial.

Dr. Chisholm told the Editors that the "North Shore continues to be my Shangri-la. I go there again and again to recharge my battery and to paint. Inspirations range from a rusty anchor to a pile of pulpwood, from a fishing dory to an aluminum canoe. The "Old Fort at Grand Portage" was done on a recent refreshing trip and at the request of the Editors."

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Letters to the Editor

Preventive Medicine

Dear Editor:

I should like to comment on the extremely pertinent article entitled "The Philosophy of Preventive Medicine" by John E. Smith, M.D., which appeared in the March issue of MINNESOTA MEDICINE.*

I agreed with much that is stated in the article. Major progress in preventive medicine in the past was largely in the field of public health including social changes and immunization programs as stated, but it is crucial to note that all of these programs could be carried out without the direct cooperation of the beneficiaries. That is, the public did not have to undergo any uncomfortable change in life style or behavior to reap these particular benefits of medical science. However, as Doctor Smith points out, the challenge today in highly industrialized societies is *health behavior.* A significant proportion of disease morbidity affecting us today is based upon life style and self-generated risk factors such as smoking, obesity, alcohol abuse, self-induced stress, and so forth. Doctor Smith certainly spoke the truth when he stated "the present state of our art is incomplete" with respect to modifying patient behavior. He then went on to state "until we learn how to do these things, we do what we can by giving acute episodic care to sick people." Doctor Smith certainly has the privilege, as does any physician, to choose to practice this sort of medicine. However, hopefully some physicians will direct their talents and energy toward improvement in the state of the art of preventing totally unnecessary illness and death.

Doctor Smith seemed to downgrade the early detection of disease. It certainly is true that it has been very difficult to demonstrate cost effectiveness of early detection and screening programs. However, these difficulties are not based so much on biological-medical factors as on the statistical and even ethical difficulties in studying large populations of patients for prolonged periods of time. One particular statement, "the worst thing about periodic physicals is that they encourage the belief that physicians can prevent disease," was disturbing to me. In the first place, no specialist in preventive medicine ever stated that the periodic physical is designed to prevent disease. One should differentiate between "primary prevention" and "secondary prevention." Primary prevention refers to the true prevention of disease as exemplified by immunization against polio. Secondary prevention does not refer to the true prevention of disease but rather to the *prevention of unnecessary morbidity and mortality* through early detection. Secondary prevention, that is the detection of disease before overt manifestation thereof, is based on the premise that it does make a difference when a physician treats a disease. If the efficacy of therapy is the same regardless at what point along the natural course of a disease it is started, then there would be no need whatsoever for an early detection system. It is doubtful that the medical profession could defend the position that early treatment is no better than late treatment. The case for secondary prevention, a major example of which is the periodic health examination, seems to be secure. However, as Doctor Smith points out, we have not yet developed optimal methodology to accomplish this purpose. This particular facet of medical practice certainly should not involve all of our energy and resources.

Most clinical practitioners, including Doctor Smith, probably practice more preventive medicine than they realize. "Routine" chest films, urinalysis, and peripheral blood counts regardless of the presenting complaint are classic examples of secondary prevention. Many other examples could be cited as well.

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*Page 196.

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I agree with Doctor Smith that many multiphasic screening programs have led to increased total health care costs and many fruitless investigations to explain "abnormalities" found during the course of screening; but failure to apply correctly the theory and principles of preventive medicine has often been the main reason for such undesirable outcomes. Well trained specialists in preventive medicine being familiar with the principles of epidemiology, systems analysis, and principles of health care evaluation usually know how to avoid such pitfalls. Doctor Smith is correct in stating that, in general, preventive health care systems cost money. What is not yet known is whether such systems can realize a net savings over a period of years. Also, preventists are really not so much interested in saving money per se as they are in reduction of morbidity and mortality.

Doctor Smith correctly pointed out that it is difficult to achieve patient compliance even with respect to "proven" therapeutic or health care regimens. But, this should not be a cause for abandonment of such programs. It should only further stimulate American medicine to meet the difficult challenge posed by the dynamics of patient behavior. Advances in the science of patient behavior could hardly be made without the direct participation of physicians working closely with psychologists, sociologists, etc.

I agree that paramedical personnel can carry out many preventive services. And, professional educators may do a better job than a clinician. On the other hand, we need physicians to determine what should be done in the first place by paramedical personnel, we need physicians to evaluate the outcome of such services, and certainly a physician is needed initially to help determine the *content* of any health educational program. The "rules for self-health" listed by Doctor Smith were excellent. And, it is pertinent that the establishment and validation of many of the rules listed depended upon research done by *physicians*. Further, this research depended heavily upon the sciences of epidemiology, biostatistics, environmental health, and behavioral sciences. It is for this reason I am concerned with the proposition that we physicians continue giving acute episodic care "until we learn how to do these things." If all physicians remain occupied with diagnosis and therapy, I'm afraid we will have no new principles to add to those 18 excellent ones listed by Doctor Smith!

Earl T. Carter, M.D., Ph.D.
Chairman
Division of Preventive Medicine
Mayo Clinic

P.S. I fear the March 8, Minneapolis Star front page account of Doctor Smith's article does a disservice to those corporations who earnestly seek to maintain the health and, hence, effectiveness of their valuable key personnel. And, I fear the article also tends to discourage persons from seeking M.D. care when poor patient compliance is a current serious problem.

Dr. John Smith's Reply

Dear Editor:

I Almost Saw a Bear

The newspapers and I have developed an arrangement. I write an article for MINNESOTA MEDICINE, exaggerating (as is my style) to make a point and then summarizing the most important points in a conclusion. The reporter ignores my conclusion, abstracts the exaggerations and has a front page-type story that attracts more attention than it deserves. I recommend the article and its conclusions but am embarrassed by the vast difference between the abstraction and my intended conclusion. I shall try to write more clearly in the future.

I thank Dr. Carter for his thoughtful comments on the article and join in his dismay over the inaccurate emphasis of the article in the *Minneapolis Star*. I am happy to note his agreement with most of the article and am not at all surprised that the Mayo Clinic assigns a high priority to executive physical examinations.

Our main difference is my feeling that providing acute episodic care to sick people is what most doctors do best, that it *is* cost effective, and that it is a very good thing to do. Of course we all practice "preventive medicine" while we are providing acute care, but my article was a reaction to the current Federal trend to downgrade the importance of acute episodic care while inflating the importance of maintaining health, preventing disease and delivering health care.

That much emphasis on health turns it into a commodity and creates an insatiable, ill-informed demand. It also fosters a belief that the more you spend, the healthier you become. Most importantly it encourages people to depend on health services to get them over every hurdle from the womb to the grave. Life becomes a series of periods requiring different therapies instead of a succession of different stages of health. People have become patients without being sick.

The new concept is that we are badly designed, fundamentally fragile and begin to die from the moment of birth. Without the professional attention of a health care system, without constant surveillance and patching up we would fall apart. We are in danger of becoming a nation of healthy hypochondriacs, living gingerly, worrying ourselves half to death; so fearful of the future that we are unable to enjoy the present. There is something fundamentally unhealthy about all this concern for health care.

I don't understand how we have become convinced of our bad health at a time when the facts are telling us the opposite. In real life we are amazingly tough, durable organisms of excellent design, full of health and with remarkable defensive and recuperative powers when disease strikes. In our favor too is the fact that most illnesses are acute and self-limiting. Most things *do* get better by morning. Most diseases are transient, reversible affairs that need little more than Grandmother's advice for getting through safely. We have all been taken in by the propaganda and it is not only bad for the spirit, but it will make any health care system, no matter how large and efficient, unworkable. If people are educated to believe they require constant medical support even for minor illnesses, and when well are still dependent on an imaginary discipline of preventive medicine, then there can be no limit to the numbers of doctors' offices, clinics and hospitals required to meet the "need."

Many moons ago when our family was younger my father-in-law got some dents in his license plate. He managed to convince the kids that it might have been a bear that chewed on the plates while the car was parked outside the cabin at Brainerd. All that Summer, whenever we went hiking, or even on the short trip to the "office" in back of the cabin, we were constantly, almost seeing the bear. "If I had gone around the next bend he might have been there . . . If I had had my flashlight, I could have seen him . . . I could hear him on the other side of the cabin but by the time I got there he was gone." In medicine there are also lots of chances to almost see a bear. "This could have turned into Pneumonia . . . You almost had a heart attack . . . Good thing you called me when you did . . ."

To teach our patients to rely this heavily on a physician is unhealthy; to begin to believe it ourselves is even worse. Statistically something may be true, but in specific cases, no one knows what lies around the next bend of the trial. For the individual no one can tell how beneficial intervention will be. The Chinese have a proverb, "It is difficult to prophesy, especially about the future." Much of what we presently call preventive medicine is merely our beginning awkward attempt to see into the future. In a fee-for-service practice the cost to the patient acts as an effective brake on this fortune telling. In a pre-pay or a no-pay situation that restraint is removed and doctors will be inundated with requests for health care and for preventive maintenance which we will be only partially able to satisfy.

To be credible we will have to develop recommendations before the financial restraints are removed and "free health care" becomes everybody's right. When anything becomes artificially priced below its market value then the demand for that product or service increases. When the cost approaches zero then the demand will approach infinity. Before that happens we will have to have some good reasons for saying, "No." Our time-honored recommendations and ways of doing things will not be applicable for the future.

With finite resources and theoretically infinite demands, medical care will have to be rationed. There is no country rich enough to provide all of the care that every individual may want. As long as doctors will have to administer the rationing program, we should become involved in planning a rational rationing process. In my assessment of personal and public priorities the care of healthy people (preventive medicine) should be far down the list.

John E. Smith, M.D.
Minneapolis, Minnesota

On Attitudinal Barriers Towards the Physically Disabled Person

Dear Editor:

Attitudinal barriers began when the first poorly developed baby was allowed to perish in the wilderness. It was a conscious, deliberate act, based on the fact that this child should not be allowed to live, for whatever reason. Now, because of man's conscience, the disabled baby is allowed to live . . . but how? where? why? and to what degree?

I had high spinal paralytic poliomyelitis in 1949, was in an iron lung for six months, still use a portable respirator at night, am confined to a wheelchair and need help with all my personal needs.

The biggest single barrier I have encountered is one of attitude, society's attitude towards me, my attitude towards both society and myself. Because I lacked physical control over my body, I felt I lacked control over my environment. I was suddenly considered by both society and myself to be an unequal, unacceptable and inferior human being who needed to be protected, controlled and segregated. I was angry about this, and resentful because I felt unable to express my anger openly, like the small child who is angry at his father but doesn't dare express it openly because the father is bigger than he is.

My chair represented my prison, a lack of hope and feeling of no value. I now recognize the prison was of my own making; it was internal, not external. I recognize that everyone, able bodied and disabled alike, have their own prisons and it is up to each one of us as to how we deal with them. I still object to the trap of the chair, but I now feel I DO have value and something to contribute, in spite of it.

I feel that the social isolation the disabled person experiences is partly a result of society's desire to put an unpleasant reminder of their own potential for mortality out of its mind. It really is not so different from the savage who discarded his baby in the wilderness. Nursing homes, special schools, lack of transportation and attendant care, architectural barriers, low quality education, lack of employment opportunities, lack of good medical care, all produce the inferiority society professes to deplore, and all are indications of society's real priorities.

It has been my experience that many times the medical profession has assumed that the disabled person needs protection because he is fragile and therefore takes on the role of a parent-child relationship. The doctor may be 'killing with kindness' because he is unaware how the disabled person really feels or how his own feelings are being sensed. He also is often more interested in the disease itself (polio, MD, etc.) rather than the specific complaint the person has come in with.

I would like the reader to participate in the evolution of a new way of life for the disabled person by supporting the following actions: (1) More exposures of a positive nature and more social interaction between disabled people and the non-disabled community. (2) Integrating the disabled child in his neighborhood public school with adequate back-up help from the school personnel so both the disabled child and the able bodied child are able to relate as equals. (3) Eliminate the idea that disability in itself creates psychological differences in people. (4) Provide disabled people with the necessary emotional, educational and political support to encourage their employment in positions of authority in areas such as health care services, counseling, public administration and political sciences. (5) Provide the disabled persons with psychological support to assist them with being at ease with themselves, which would have the effect of placing other people at ease also. (6) Actively encourage the dissemination of information by the disabled person regarding the attitudinal, architectural and societal barriers that presently exist in society. (7) Emphasize the positive aspects of the disabled person's uniqueness, of being themselves, which would de-emphasize the effects of 'peer pressure.' (8) Establish and foster positive intellectual, academic and psychological expectations for the disabled person.

Accept us and help us to accept ourselves. Allow us to step out and be counted and to take part in community life. Permit us to make our own mistakes and take our own lumps. Encourage our integration into society as much as our physical limitations allow.

Leah J. LaBar
Minneapolis, Minnesota

Harold A. Diehl Award

The committee for the Diehl Award given annually by the Minnesota Medical Alumni Association solicits nominations for this award from the physicians of Minnesota. The award is presented to one or more physicians meeting these four major criteria:

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Nominations for the 1976 awards should be sent immediately to:

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(Continued to page 418)

Legislation

If We Had Not Been There . . .

"What have they done for us lately?" Often asked of politicians we find ourselves asked this same question with increasing frequency as physicians attempt to assess the value of their professional associations. We will try to provide an overview of one aspect of your organization's many and varied activities—legislation. We will describe the "flavor" of this past session of the Minnesota legislature and recount what could have happened if MSMA, through your membership dollars, had *not* been there.

This past legislative session was unique in a number of ways. Perhaps best described as generally consumer oriented and sometimes naive, the House of Representatives consisted of more first termers, youth, women, and DFLers than at any time in history. Democrats outnumbered Independent-Republicans by a margin of 103 to 31. More significantly, of the 27 members of the House Health and Welfare Committee, 16 were freshmen with whom we literally had to "begin from scratch" as we attempted to inform them of medicine's views on the broad spectrum of health related issues. The Senate was somewhat more evenly balanced politically than the 37 to 29 DFL advantage would suggest, as Conservative Democrats frequently joined with Independent-Republicans on normally partisan votes. The entire legislature itself was still reaching for its proper role in an "even year" session. Initially thought and presumed to be a short non-spending clean-up period the 1976 session soon became full-blown ending on a note of discord between the Senate and House leadership. The procedural rule book was all but forgotten making tracking and monitoring of medically related legislation a most difficult and arduous task. Bills that had been defeated in committee were amended into unrelated proposals; conference reports became "Christmas trees" or "garbage bills" (depending on your point of view) and committee action on conference reports was finalized in some instances without the members even meeting despite the openness in government theme which we have heard so much about.

Jim Sova, on the right, chief Minnesota State Medical Association lobbyist and Director of the Department of Governmental Affairs, discusses legislative strategy with Field Representative, Rick Teske, before entering the Capitol building.

With the 1976 elections looming large, most business and professional organizations felt the cutting edge of election year rhetoric. Health care delivery and costs continued to be exploited as political issues contributed measurably to the large number of medically related bills. Of some 5,000 bills introduced into the Senate and House, MSMA reviewed, monitored, or otherwise became involved in almost 500 or 10% of all bills introduced. While MSMA attempted to "diagnose" each issue, it obviously could not actively participate in the "treatment" of each piece of legislation. The sheer number of bills dictated that priorities be set and primary attention directed to perhaps 40 or 50 of the more important issues lest our efforts be spread so thin as to be rendered virtually ineffective in all areas. Policy and priorities are established by the MSMA House of Delegates, Council and/or Executive Committee.

Implementation of our legislative effort on the Hill then becomes the responsibility of many persons. In addition to MSMA lobbyists, Jim Sova and Rick Teske, it consists of physician contacts for each legislator, supportive staff research, physician testimony at committee hearings plus input from the Public Policy and other MSMA Committees whose purview may include legislation. Together they are your "organized medicine" effort working not only with the legislature but state and federal agencies, insurance companies, and almost any other quasi-political group that may influence the delivery of medical care. In addition, we coordinate our activities and work with the various medical specialty organizations in the state and on many issues with other health related professional organizations.

Success (or failure of our legislative effort rests to a large degree on how well individual physician legislative contacts have functioned at the grass-roots level. On many of the key issues we either won or lost on a basis of the amount of direct physician contact legislators received. As a measure of our ability to influence legislation, we are able to report that very few major pieces of legislation which medicine opposed were passed. Before we applaud too loudly, we must say that a number of bills which we supported (particularly in the area of malpractice) did not succeed.

Against this legislative backdrop how well did medicine fair in this 69th session of the Minnesota legislature? What would have happened if we had not been there?

If We Had Not Been There, You Would Have Had:

- A Board of Medical Examiners controlled by consumers.
- Strept throat cultures taken, incubated and read by school nurses for all students and their families.
- The Commissioner of Insurance given regulatory authority over malpractice insurance rates and the power to potentially drive out our few remaining professional liability carriers.
- Health insurance companies given subrogation rights against successful malpractice claimants thus encouraging initiation of additional lawsuits.
- Severe restrictions on the use of collection agencies and dunning by health providers.
- A possible statutory requirement that all hospital based physicians be salaried and precluded from direct billing.
- Social workers and other non-physicians interceding in the physician-patient relationship to discuss alternatives to commitment with hospitalized mentally ill patients.
- A statewide breast cancer screening diagnosis and treatment program without the involvement of the patient's private physician.
- Certain ambulatory out-patient facilities and physicians' offices included under the Certification of Need Act.
- A licensure bill for nurse anesthetists which would have prohibited degree program anesthesia assistants from being utilized in Minnesota or Physician-Assistant programs in anesthesia from being developed.
- Counties able to deny free choice of medical provider for patients on general relief.
- No Joint Underwriting Association (JUA) that would make professional liability insurance available in the event that significant gaps in malpractice insurance coverage exists.
- The Commissioner of Welfare rather than a peer review organization unilaterally determining whether or not certain procedures were medically necessary or charges excessive in determining reimbursement under the Catastrophic Health Insurance Act or fraud under the Medical Assistance Program.
- The Commissioner of Health directly appointed by the Governor to serve at his pleasure rather than the State Board of Health.
- Continuing medical education requirements for relicensure set forth by legislative dictate or the Higher Education Coordinating Committee rather than the State Board of Medical Examiners in conjunction with MSMA.
- A state administered malpractice screening panel whose non-binding decisions would have given plaintiffs two chances at success rather than the MSMA/Bar Association program for voluntary-binding arbitration.

You should realize there were many more bills that MSMA supported, opposed, or attempted to modify in conjunction with other organizations. With issues such as Catastrophic Health Insurance, community health services, DWI legislation, abortion regulation, hospital rate regulation, etc., we had a direct impact but were not solely responsible for the outcome of the legislation. Next year we will see many of the same items discussed again. If we are to be successful we will need greater physician activity in campaigns and legislative activities. Without physicians and their spouses taking an active part in selling our legislative program, no amount of staff can persuade legislators of the need for or opposition to any proposal. Considering the confusion and climate of this past legislature, we must interpret the outcome for medicine and public health overall as a success. Did you get your money's worth? Only you can decide.

C. A. Anderson, M.D., Chairman
Committee on Public Policy

This will be the last article written by the Chairman of the MSMA Committee on Public Policy. This Committee is to be dissolved and its function absorbed into a new Legislative Committee with an expanded role under the newly formed MSMA Division of Socio-Economic Affairs.

Physicians desiring additional information on particular legislation, specific bills or a copy of the MSMA Legislative-Wrap Up Bulletin #13 should write or call the MSMA office Division of Socio-Economic Affairs, 900 American National Bank Building, 101 East Fifth Street, St. Paul, Minnesota 55101, 222-6366.

Request for Physician's Art Work

For many years the Board of Editors of MINNESOTA MEDICINE has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers have received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Pictures will be returned if identified with the name and address of the physician. Please submit your picture as prospective cover subjects to the Editor of MINNESOTA MEDICINE, 375 Jackson St., St. Paul, Minnesota 55101.

During 1976 the Editors would like to pay homage to the Bicentennial by having our covers depict places, events, scenes, etc., that have historical or patriotic significance for the State of Minnesota. Please keep the Bicentennial theme in mind when submitting prospective covers for 1976.

Farrell Stiegler, M.D.
Cover Editor

Book Reviews

JOURNEY by Suzanne and Robert Massie. A. A. Knopf Co., New York, 1975. Price $8.95.

The title of this book depicts its message: the journey through life of a hemophiliac and its many ramifications. The book is beautifully written by the parents; it reflects frustrations, intensities, tears, determination, and deep love. Well equipped to author such a book because of their backgrounds as writers, the Massies vividly depict the difficulties and experiences of a chronic disease. The authors and their son, whom I was fortunate to meet during a hemophilia symposium in 1974, tell a story worth reading. Rarely does a nonfiction narrative compel the reader to not put down the book until its 417 pages are concluded. The authors of *Nicholas and Alexandra* show excellent medical expertise and research efforts in reporting the story and of modern hemophiliac care.

Descriptions of the parent's thoughts at the time of diagnosis, their responses to the oft noted coldness of the medical profession, and their futile efforts to "afford" the disease are well shown. However, the story reflects much more than that. It paints a picture of their valiant attempts to raise a son capable of participating normally in society. Economic, psychologic, and humanitarian views are expressed which often, we the professional, may not sufficiently realize. Decisions as to whether or not to continue a family in spite of a genetic disease and the responsibility of funds for a disease costing $5000-$10,000 a year in the United States are presented. This, in turn, asks the reader to reexamine his own moral and ethical views. The self analysis, personalities, and strengths of each parent is explored. The Massies' son Bobby, now 18, offers insight into his world.

A major anger is expressed (and rightfully so) that this the richest country in the world, can charge for blood products that are donated while encouraging free donation of organs for transplantation. This, while the other major countries of the world aid their populations with catastrophic insurance, medical services, and blood. The American Red Cross is painted as not the great benefactor that we are lead to believe that it is, and Hyland Laboratories, a drug company, is severely chastised for its profit making commercial views. Even the National Hemophilia Foundation is taken to task for some of its early policies and parent aids.

It would seem that any other chronic disease could be substituted for hemophilia in this book and yield a similar message of importance. Admiration for this family and others with chronic diseases reaches a new high after this book's message.

Lawrence J. Singher, M.D.
Minneapolis, Minnesota

MEDICAL PHYSIOLOGY by William F. Ganong, 587 pp, $10.50, Los Altos, California; Lange Medical Publications, 1975.

This book is an excellent, readable, physiology textbook. It is written in a concise, precise fashion which is uncluttered with footnotes and lengthy discussions of primarily historical interest.

The illustrations are excellent and always pertinent. Schematic diagrams are correlated with photographs and artistic illustrations. The author makes excellent use of pathologic physiology to enlarge upon his discussions of normal mammalian physiology.

This book is of an interesting, fast-moving quality. This reviewer recommends this book to any physician interested in reviewing physiology, either in specific areas or in general. Because of its uncluttered quality the Review of Medical Physiology is an excellent text for medical students also.

Richard R. Owen, M.D.
Minneapolis, Minnesota

IN DEFENSE OF THE BODY: AN INTRODUCTION TO THE NEW IMMUNOLOGY, by Rodger Lewin, Anchor Books, 1974, 146 pages, $2.50.

I enjoyed this book because it clarified "new immunology" for me.

Like many who casually follow the immunological scene, I knew exciting things were going on. I was aware of: (1) the worldwide commercial push to come up with precise immunological tests to screen for and to monitor cancer: (2) the growing use of immunological cell typing and immunosuppressive agents in transplant surgery and in cancer therapy; (3) the introduction of such tests as immunoelectrophoresis and immunoglobulin assays into clinical laboratories; (4) the evolution of an as yet undefined field known as "clinical immunology" and (5) the excitement over recent studies using sheep red cells to distinguish between thymus-derived "T" lymphocytes from bone marrow-derived "B" lymphocytes.

Finally, I was conscious that Doctor Robert Good, first of the University of Minnesota and now of Sloan-Kettering Institute conceived and confirmed many basic ideas of the "new immunology."

But I did not have a sure grasp of how all the ideas and events fitted together. This book makes the story whole. The author, Rodger Lewin, a biochemist who serves as Science Editor of *New Scientist,* has written a clear exposition of the history of immunology, its recent resurgence, and Good's role.

If you want to be well-informed about the rudiments of modern immunology, I encourage you to start with this paperback primer.

Richard L. Reece, M.D.
Editor-in-Chief

Grand Rounds

Heat Stroke

ROGER RALSTON, M.D.[*]

The basic physiology and pathogenesis of heat-induced injury are discussed with special emphasis upon the morphologic and functional changes in the organ systems usually compromised by heat stress: CNS, cardiovascular, hematologic, and renal.

HEAT STROKE is a symptom complex produced by excessive body heat. It occurs in many clinical settings. It is a medical emergency; but because it presents in different ways, physicians may fail to recognize and treat it promptly. Yet an uncomplicated outcome depends on rapid treatment. This treatment, in turn, depends on understanding the physiology of heat stroke.

History

Heat-related disorders have probably afflicted man since he has lived in temperate climates. Heat stroke was recognized and recorded very early. There are biblical references to death from heat stroke.[1] In 24 B.C., a Roman military expedition was annihilated in Arabia during a heat wave. A description of the disease, then known by the Greeks as "Siriasis" (after the dog star Sirius, which follows the summer sun) is compatible with heat stroke.[2] The writings of Middle Europe in the 15th to 18th centuries contain accurate accounts of clinical manifestations including a particularly detailed and gruesome account of the death of 11,000 in the streets of Peking during a heat wave from July 14-25, 1743.[3]

More recent recordings of heat stroke have involved military recruits. Two well-studied examples occurred in the Southern United States in 1943-1945[4,5] and in Israel in 1956-1966.[6]

Industry-related epidemics occur, and in most places the incidence has declined markedly by recognizing and eliminating predisposing factors. The best studied cases are among the Bantu gold miners in the Transvaal and Orange Free State.[7] Here 300,000 native Africans per year are involved in strenuous physical labor at depths of 4,000 to 11,000 feet and ambient air temperatures of 95 to 105° F. with relative humidities usually in excess of 90%.

Mass civilian casualties have also been reported in association with heat waves.[8] During the 1959-1961 pilgrimage to Mecca, heat illness accounted for 1,025 deaths among 1,250,000 pilgrims.[9] During the summer months of 1952 to 1954 more than 100 patients per month were seen at the St. Louis City Hospital for heat-related disorders.[10] These were three of the six hottest summers in the last one-hundred years. Over this three-year period, 178 patients with heat stroke were admitted and 12 died. In Detroit, during the successive heat waves of 1962-1963, there was a sharp increase in death from heat illness and cerebrovascular and cardiovascular diseases.[11] These latter deaths probably reflect the inability of the elderly population with minimal cardiovascular reserve to respond to heat stress.[8] During a two-week period in 1966, there were 25 deaths from 200 cases of severe heat disease seen at the King's County Hospital in Brooklyn.[12]

Classification

According to the Eighth Revision of the International Classification of Diseases, there are seven distinct syndromes associated with excess body heat (Table).[13] For clinical purposes it is convenient to group these disorders into three clinical syndromes.

TABLE

Heat Related Disorders

922.0	Heat Stroke
922.1	Heat Syncope
922.2	Heat Cramps
922.3	Heat Exhaustion, Anhidrotic
922.4	Heat Exhaustion Due to Salt Loss
922.5	Heat Exhaustion, Unspecified
922.6	Transient Heat Fatigue
922.7	Heat Edema
922.9	Other Heat Effects

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[*] Medical Resident, Hennepin County Medical Center, Minneapolis, Minnesota.

Edited by: Arthur Leonard, M.D , F.A.C.P. Coordinator, Medical Education and Attending Physician, Department of Medicine, Hennepin County Medical Center.

I. *Heat Cramps:* A syndrome of mild muscle pain associated with profuse sweating without increased temperature, thought to be due to salt imbalance.

II. *Heat Exhaustion:* A syndrome of hypotension, mild CNS symptoms (irritability, dizziness, faintness, anorexia), nausea and vomiting, with or without increased temperature. This is thought to be secondary to water and electrolyte disturbances in response to body requirements for heat dispersal.

III. *Heat Stroke:* A syndrome of marked CNS dysfunction associated with an inability of the normal homeothermic mechanisms to maintain body temperature.

Heat stroke is the most severe of the syndromes of heat disease with a reported mortality of 15 to 60%.[1,6-8,10,12]

Note the absence of reference to the patient's level of consciousness. Although most patients present with depressed consciousness, the CNS dysfunction varies from severe agitation to coma with recurrent seizures. Neither is the level of body temperature included, although it is usually markedly elevated. When body temperature is first measured, patients may have been moved from the stressful situation and, if thermoregulatory processes are still working, the body temperature may have fallen dramatically.

These clinical syndromes are distinct and independent. Patients seldom progress from heat cramps to exhaustion to heat stroke. Heat cramps and exhaustion are metabolic consequences of dealing with the stress of heat, while heat stroke is caused by failure to control body temperature with direct toxic damage from heat.

Physiology

All homeothermic animals including man are able to maintain body temperatures within a narrow range despite wide fluctuations in environmental conditions. For young adult medical students at rest, the mean oral 9 a.m. temperature is 36.73 ± 0.47° C. (98.1° F.).[14] Rectal temperatures average 0.65°C. (1.2°F.) higher. These both approximate the body "core" temperature or the temperature of the cranial, visceral, and thoracic cavities and most of the body's muscle mass. A diurnal variation of 1°C. (1.8°F.) exists with the highest temperatures in the late afternoon and the lowest in the early morning.[15] This presumably reflects the level of body activity and reverses with inversion of the sleep-wake cycle.[18] Maintaining normal body temperature is a complicated process involving nearly all organ systems. Basically, it is a balance between the heat accumulation and dispersal mechanisms.

Radiation, convection, and evaporation result in heat energy dispersal. Conduction and elimination via wastes do not contribute significantly. At resting conditions (room temperature of 68° F.), about 66% of heat loss is via radiation, 15% by convection, and 19% by vaporization.[16] Radiant energy from the human body lies in the infrared spectrum, making man a perfect absorber and emitter of infra-red energy with a minimum of reflection or translucency.[17] As environmental temperature approaches skin temperature, the absorption of environmental infra-red radiation rapidly approaches emission. When the two are in equilibrium, no radiant heat loss is possible. Similarly, when the surrounding environmental temperature is equal to the skin temperature, no heat exchange takes place by conduction or convection.[18] Under these conditions, losses from vaporization are still possible, provided the relative humidity is less than 100%. The average heat of vaporization for the human body is 580 Kcal/Kg loss of vaporized water.[15] This represents heat loss due to cooling action of evaporation plus that due to the heat carried from the body in the vapor itself.

Under normal basal conditions at room temperature (68 to 70° F.) man secretes little or no sweat; yet, the average loss by vaporization is 30 gm of H_2O/hour or 17.4 Kcal/hour (30 gm/hour x 580 Kcal/Kg = 17.4 Kcal/hour). This represents 19% of the normal basal body heat loss. This "insensible loss" is composed of respiratory tract losses from the nasal and pharyngeal mucosa, the epithelium of the tracheobronchial tree, and interstitial fluid vaporization from the dermis before it reaches the skin. Humidity and respiratory minute volume affect the interstitial vaporization. The respiratory losses depend on capillary circulation. Conditions such as dehydration, shock, hypotension, and low cardiac output as well as dermal vasoconstriction secondary to local cooling and autonomic drugs inhibit this loss.[14-17]

When the heat lost by radiation, convection, and insensible losses is inadequate to prevent an increase in body temperature, or when the processes cannot operate effectively, the necessary loss of heat from the skin depends on sweat gland activity, fluid secretion, and subsequent vaporization. In man there are about 2.5 x 10^6 sweat glands, each innervated by cholinergic receptors. Sweat is formed and secreted from the basal cells of the eccrine sweat glands. Their capacity to secrete water depends on blood flow and increases with cutaneous vasodilatation.[19,20] The relative ability to sweat per unit body weight decreases with obesity, which decreases the surface area to body weight ratio. At low sweat flow rates, the fluid is a dilute ultrafiltrate of plasma; but as the rate of sweating increases, the salt concentration approaches that of plasma. The increased heat required for vaporization (colligative properties) is insignificant.

Sweat cools only if the water of this solution vaporizes. Sweat that is wiped or drips from the body carries an insignificant amount of heat.

The cooling capacity of human sweat depends on surrounding vapor pressure and may be very great. A dramatic illustration is the absence of ill effects in healthy young male volunteers exposed to a dry atmosphere at 250°F. for 15 minutes. A beef steak was cooked under the same condition.[21]

Circumstances that inhibit sweating or prevent vaporization may impede heat loss. Anatomic skin abnormalities such as icthyosis, congenital ectodermal dysplasia, scar tissue from burns, and scleroderma prevent sweating.[22,23] Ointments, occlusive dressings and clothing do likewise. Decreased cardiac output from shock, hypotension, dehydration, or decreased capillary flow secondary to direct physical skin cooling or generalized cutaneous vasoconstriction secondary to pressor amines, e.g., levarteranol, decreases sweating.[20]

Physical constraints that prevent air circulation, including vapor barrier suits of astronauts, jet pilots, and deep sea divers, vinyl weight reducing "sweat suits," and closed non-air-conditioned spaces including auto trunks, semi-trailer trucks, and living quarters have all been associated with heat stroke.[1] Even heavy draping for sterile fields in surgery has been shown to prevent heat loss and may contribute to malignant hyperthermia.[26]

Pharmacologic inhibition of sweating is common and occurs with many drugs. This results from their ability to block or inhibit the parasympathomimetic (muscarinic) effects of acetylcholine.[27] The most potent of these drugs is atropine. Related drugs including scopolamine, homatropine, benztropine (Cogentin®), and propantheline (Pro-Banthine®) have similar effects.[24] In addition, antihistamines, major tranquilizers, and anti-Parkinsonian drugs have similar chemical structures with active ester subgroups and retain atropine-like side effects.[27] There are reports of heat stroke in elderly patients receiving anti-psychotic and anti-Parkinsonian medication in the absence of other known predisposing factors.[24-26]

Clinical Pathologic Picture

Onset

The onset is usually acute (71%) with a few patients having a prodrome lasting minutes to hours (21%), and, occasionally, days (8%). With the prodrome, the symptoms are due to electrolyte shifts, dehydration, and lactic acidosis as a result of physiologic responses of heat dispersal. Most prominent are lethargy, confusion, weakness, cerebellar dysfunction, and muscle cramps.[4] More commonly, the patients present acutely without warning.

Vital Signs

The body temperature is usually elevated to levels not commonly seen in other conditions. In the largest series available, 104 of 125 patients with heat stroke had initial temperatures greater than 106° F.[4] Many patients have been reported to survive temperatures of 108-110°F., and the usual upper limit of human survival is considered to be 112°F.[15] Unfortunately, most clinical thermometers only measure to 108° F. and data on temperatures above this are not available. If the patient is seen some time after the period of maximal heat production, the temperature may be minimally elevated. This is especially true when emergency first aid cooling is carried out.

With treatment the temperature falls over a period of hours. Occasionally, mild temperature elevations reappear; but these should lead to suspicion of infection or hypothalamic damage.

Tachypnea is usually present initially, but often is replaced by Kussmaul or Cheyne-Stokes breathing. The pulse is usually rapid and weak. Hypotension and shock are common but not universal.[6,10]

CNS Disturbances

Disturbances of the central nervous system are present in all cases. The level of consciousness is often depressed with coma, stupor, or delirium being present. Persisting coma in spite of return to normothermia is a poor prognostic sign. Seizures occur in approximately 60% of cases and, as with coma, are present in most fatal cases.[4,6,10] Signs of cerebellar dysfunction are prominent and may persist. Pupillary changes, decerebrate positioning and incontinence are frequent. Irritability, lack of concentration, disorientation, delusions, and hallucinations occur.[6,33,34] Complete return of normal neurologic function occurs in most survivors, but cases of persisting cerebellar dysfunction, hemiplegia, aphasia, and emotional instability are known.[34] Lower motor neuron and peripheral sensory nerve lesions occur less frequently.

Autopsy studies[4,10] reveal edema of the brain and meninges with flattening of the convolutions and the presence of a cerebellar pressure cone. Petechiae are common in the walls of the third and fourth ventricles. Microscopic examination reveals cortical edema and congestion with degenerative changes in the neurons. Glial proliferation is prominent in cases surviving longer than 24 hours. The basal ganglia have similar but less severe changes. Cerebellar changes are more consistent and develop more rapidly than in any other part of the brain. The Purkinje cells become edematous and degenerate. Gliosis occurs early and is severe.[35] Surprisingly, the hypothalamus is relatively spared with no light microscopic changes noted.[4,6,35] Most authors[4,6] believe the cellular changes are the result of hyperthermia whereas hemorrhages, congestion and edema are the result of shock and/or clotting abnormalities.

Cardiovascular

The circulatory collapse seen in heat stroke is not well understood. Excessive circulatory requirements appear to be related to two principal mechanisms. The first is cutaneous vasodilatation, a normal compensatory mechanism for heat dispersal.[16] The second is reduced total peripheral resistance as a result of the elevated metabolic rate and oxygen requirements.[36] This persists in spite of normothermia and resembles the phenomenon of compensatory hyperemia after ischemia.[37] The result is a demand for marked increase in cardiac output.

Hemodynamic studies in young healthy adults reveal cardiac output and myocardial oxygen requirements double as the temperature is increased from 98 to 107° F.[14] Above this temperature the heart fails rapidly, both in isolated perfused myocardial strips[38,39] and in experimentally induced heat stroke.[36] Epinephrine initially reverses some of this failure[38] and isoproteronol has been used with some success clinically.[36]

A third possible mechanism is the presence of an elevated pulmonary vascular resistance, suggested by the increased pulmonary vascular congestion and edema as well as the dilatation of the right heart found at autopsy.[4,39] Microscopically, there is hemorrhage in 20% of fatal cases. This is usually confined to the left side of the intraventricular septum.[4,40,41] Massive myocardial hemorrhage may be seen,[4] and myocardial infarction in the presence of normal coronary arteries has been described.[40]

Hematologic

Clinical and laboratory evidence of bleeding disorders is common. Petechiae and hemorrhages occur in all parenchymal organs, in the skin and in the gastrointestinal tract.[4] Oozing from venipuncture sites is observed. Electron microscopic studies reveal severe capillary endothelial cell damage, aggregation of platelets and capillary micro-thrombi in many organs.[42] Hypoprothrombinemia,[6,43] hypofibrinogenemia,[6] thrombocytopenia,[44] and intravascular hemolysis,[45] may be found and suggest disseminated intravascular coagulation.[46,47] Heparin therapy has been used with prompt cessation of clinical hemorrhagic manifestations and a return to normal levels of Factor V, Factor VII, fibrinogen, and platelets.[46]

Musculoskeletal

In cases of heat stroke associated with vigorous physical exercise or complicated by generalized seizure activity, necrosis of skeletal muscles and myoglobinuria may occur.[48] Potassium depletion, whether from diuretic therapy or secondary to hyperaldosteronism in response to salt loss from sweating,[49] predisposes to a higher incidence of and more severe necrosis.[50-53] Potassium is released from contracting skeletal muscles,[49] and its rising concentration in interstitial fluid is thought to dilate arterioles.[55] Thus, with potassium deficiency, exercise is not accompanied by a sufficient muscle blood flow and rhabdomyolysis may occur secondary to local ischemia.[50]

Clinically, this is manifested by profound muscular weakness, tenderness, and severe myalgia.[48] It may be accompanied by elevated enzymes of muscle cell origin (CPK, aldolase, SGOT, LDH) and myoglobinuria.[48,56,57] The course in survivors is usually one of slow recovery of muscle strength over a period of months.[48]

Renal

Acute renal failure in heat stroke was first documented in a review of 125 cases of death from heat stroke during World War II.[4] Subsequent reports fail to explain its pathogenesis.[7,37,58] The damage is mild in most patients,[7] but in about 10% it is severe. Several etiologic factors have been proposed. Widespread tissue injury suggests direct thermal damage. Decreased renal plasma flow secondary to hypotension and peripheral vasodilatation undoubtedly contributes. Secondary disturbances such as hyperuricemia, acidosis, and pigmenturia, probably play a role. The clinical picture is usually that of acute oliguric renal failure.[7,10] Pathologically, there may be tubular necrosis, pigment casts, or no detectable histologic changes.[59] Attention to hydration and increasing urine flow with diuresis may be helpful in some cases.[60]

The acute hypercatabolic state may make frequent dialysis necessary. The clearance rates of potassium and urea with peritoneal dialysis may not be sufficient to control hyperkalemia and uremia necessitating frequent hemodialyses.[61] The clinical course is similar to acute renal failure from any cause and is dependent upon co-existing disease and adequate management. In most cases, recovery without residua can be expected, but cases of chronic progressive interstitial nephritis without obvious cause (e.g. diabetes mellitus, analgesic abuse, gout, heavy metals, radiation, or bacteruria) have been reported.[62] This may be a consequence of disseminated intravascular coagulation with capillary fibrin plugs leading to ischemia and progressive scarring.[63]

Hepatic

Liver damage accompanies many cases of heat stroke. This was first reported in 1937 in MINNESOTA MEDICINE[64] and has been noted in many reports of heat stroke and fever therapy since.[65] Typically, jaundice appears after one to three days and resolves over a period of weeks. Serum enzymes of hepatic origin (SGOT, LDH, alkaline phosphatase) and bilirubin are usually elevated. Prothrombin and albumin levels are depressed.[6] Physical examination may reveal an enlarged tender liver, lethargy, and asterixis.[40,65,66] Histologically, there is congestion with centrolobular zonal necrosis.[4,10,67,68] Shock, passive congestion and hypoxia undoubtedly contribute to damage, but heat alone has been shown to cause significant liver cell dysfunction in experimental models.[69,70]

Dermatologic

Interest has centered on the role played by skin and sweat glands. Case reports document the marked absence of sweating in many cases.[4,10] This is attributed to a failure of CNS temperature regulation.

Physiologic studies demonstrate reproducible sweat gland fatigue. Repeated exposure to heat changes electrolyte composition and volume of sweat. Light and electron microscopy demonstrate the depletion of glycogen stores of the secretory coil and ducts after a single episode of sweating. Repeated episodes cause major structural alterations with degeneration (shrinkage, vacuolization, and fusion) of the basal cells of the eccrine sweat apparatus.[19,71] Studies in victims of heat stroke with anhydrosis confirm these findings.[19,72]

Pulmonary

Vascular congestion, alveolar and interstitial edema and hemorrhagic infarcts may occur.[4,10] In less severe cases respiratory insufficiency is not a problem but bacterial pneumonia often occurs in those requiring ventilatory support.[1,6,12]

Other significant tissue damage may include isolated focal necrosis and hemorrhage in the pancreas, adrenal cortex, spleen, conjunctiva, small bowel or colon.

Treatment

The goal of treatment is to reduce the heat load and supplement heat dispersal mechanisms. Immediate treatment should include support of vital function and restoration of normothermia. Measures to prevent seizures and shivering should be initiated at once.[73] Infection, bleeding disorders and renal failure should be sought and treated. The presence of any pre-existing illness, the severity of the insult and initiation of prompt and adequate therapy determine the prognosis. In young, previously healthy individuals, expect complete recovery.[1,6,10]

References will be found on page 430.

Testing in Humans: Who, Where & When.

te weight of ethical opinion:

Few would disagree that the effective-
s and safety of any therapeutic agent
evice must be determined through
ical research.

But now the *practice* of clinical re-
ch is under appraisal by Congress, the
ss and the general public. Who shall
inister it? On whom are the products
e tested? Under what circumstances?
how shall results be evaluated and
ized?

The Pharmaceutical Manufacturers
ociation represents firms that are sig-
cantly engaged in the discovery and
elopment of new medicines, medical
ices and diagnostic products. Clinical
arch is essential to their efforts. Con-
uently, PMA formulated positions
ch it submitted on July 11, 1975, to
Subcommittee on Health of the Sen-
Labor and Public Welfare Committee,
s official policy recommendations.
e are the essentials of PMA's current
king in this vital area.

1. PMA supports the mandate and
sion of the National Commission for
Protection of Human Subjects of
medical and Behavioral Research and
rs to establish a special committee
posed of experts of appropriate
iplines familiar with the industry's
arch methodology to volunteer its
ice to the Commission.

2. PMA supports the formation of an
pendent, expert, broadly based and
esentative panel to assess the current
e of drug innovation and the impact
n it of existing laws, regulations and
cedures.

3. When FDA proposes regulations,
ould prepare and publish in the *Fed-*
Register a detailed statement assess-
the impact of those regulations on
g and device innovation.

4. PMA proposes that an appropri-
y qualified medical organization be
uraged to undertake a comprehen-
study of the optimum roles and
onsibilities of the sponsor and physi-
when company-sponsored clinical
arch is performed by independent
ical investigators.

5. PMA recognizes that the physician-investigator has, and should have, the ultimate responsibility for deciding the substance and form of the informed consent to be obtained. However, PMA recommends that the sponsor of the experiment aid the investigator in discharging this important responsibility by providing (1) a document detailing the investigator's responsibilities under FDA regulations with regard to patient consent, and (2) a written description of the relevant facts about the investigational item to be studied, in comprehensible lay language.

6. In the case of children, the sponsor must require that informed consent be obtained from a legally appropriate representative of the participant. Voluntary consent of an older child, who may be capable of understanding, in addition to that of a parent, guardian or other legally responsible person, is advisable. Safety of the drug or device shall have been assessed in adult populations prior to use in children.

7. PMA endorses the general principle that, in the case of the mentally infirm, consent should be sought from both an understanding subject and from a parent or guardian, or in their absence, another legally responsible person.

8. Pharmaceutical manufacturers sponsoring investigations in prisons must take all reasonable care to assure that the facilities and personnel used in the conduct of the investigations are suitable for the protection of participants, and for the avoidance of coercion, with a respect for basic humanitarian principles.

9. Sponsors intending to conduct non-therapeutic clinical trials through the participation of employee volunteers should expand the membership and scope of its existing Medical Research Committee, or establish such an internal Medical Research Committee, with responsibility to approve the consent forms of all volunteers, designs, protocols and the scope of the trial. The Committee should also bear responsibility to ensure full compliance with all procedures intended to protect employee volunteers' rights.

10. Where the sponsor obtains medical information or data on individuals, it shall be accorded the same confidential status as provided in codes of ethics governing health care professionals.

11. PMA and its member firms accept responsibility to aid and encourage appropriate follow-up of human subjects who have received investigational products that cause latent toxicity in animals or, during their use in clinical investigation, are found to cause unexpected and serious adverse effects.

12. PMA supports the exploration and development by its member companies of more systematic surveillance procedures for newly marketed products.

13. When a pharmaceutical manufacturer concludes, on the basis of early clinical trials of a basic new agent, that a new drug application is likely to be submitted, a proposed development plan accompanied by a summary of existing data, would be submitted to the FDA. Following a review of this submission, the FDA, and its Advisory Committee where appropriate, would meet with the sponsor to discuss the development plan. No *formal* FDA approval should be required at this stage. Rather, the emphasis should be on identification of potential problems and questions for the sponsor's further study and resolution as the program develops.

The PMA believes that health professionals as well as the public at large should be made aware of these 13 points in its Policy on Clinical Research. For these recommendations envisage constructive, cooperative action by industry, research institutions, the health professions and government to encourage creative and workable responses to issues involved in the clinical investigation of new products.

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Classified Advertisements

(Continued from page 406)

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(Continued to page 434)

Infant/Preschool Hearing Impaired Child

Early Public School Intervention Emphasizing Parent Training

WINIFRED H. NORTHCOTT, Ph.D.*

Individual hearing aids and a parent-oriented public school auditory-oral education of deaf children from birth to four years are central to the child's effective use of residual hearing for language acquisition and social competence. Many children labelled deaf by audiogram can receive their education in regular classes in later years.

TODAY IN MINNESOTA, *Deaf Children Are Learning to Hear*† at an increasingly early age. This is not by chance. During the last decade, the medical, educational and legislative climate in our state has been increasingly hospitable to the principle of very early detection of hearing loss and referral to an educational program for remediation.

As a result, an increased number of hearing impaired children are entering regular classes in their neighborhood schools following the early fitting of hearing aids and "graduation" from a formal *public school-sponsored* infant/preschool educational intervention program which offers support to the family as well. There is clear evidence that the *degree* of physiological loss of hearing, as indicated on an audiogram, is not a valid predictor as to who is or is not a candidate for assimilation in this learning environment.

Who Is Deaf?

The incidence of deafness in the general population is low. The Bureau of Education for the Handicapped, U.S. Office of Education, lists an incidence of 0.075 or three individuals in 4,000 children of school age who are deaf (91 d.b. ISO or greater) and 0.5 or one in 200 children who are hard of hearing. In the instance of preschool children, the Bureau suggests that 50% of this incidence figure in the general population be considered as a more realistic one due to the present delay in identification and referral to a formal educational program.

The term *hearing impaired* is popular today as a generic classification which indicates a hearing loss ranging from mild to profound as measured by an audiogram. It is valuable because it is neutral in emotional content and in the instance of a very young child, permits the family and special educators to observe carefully the response to full time hearing aid usage and training in the dynamic use of residual hearing as a natural component of daily activities in the child's home. "What can he hear?" "What can he do?" cannot be answered quickly.[16]

The term *deaf* is applicable to children in whom the sense of hearing is nonfunctional for ordinary daily use in communication, with or without a hearing aid; this can only be determined after systematic attention to the development of listening skills. In terms of the dynamics of the "self fulfilling prophecy," responding to children with different degrees of loss as if they were *"deaf"* leads to outcome behavior in the predicted direction.[1]

The term *hard of hearing,* as the word *deaf,* is also subsumed under the general classification *hearing impaired.* It is a label used to describe individuals with enough residual hearing, generally with a hearing aid, to use it as the primary modality for the acquisition of language and proficiency in speech communication with others.

Hearing Aids for Young Children

The statistical validity of definitive tests of hearing in neonates and infants[2] supports the early prescription of wearable hearing aids, with binaural aids being increasingly preferred over monaural ones.[3] The assumption that a young child with normal intelligence and an intact central nervous system who may be *deaf* by audiogram, can learn to rely on the auditory channel for linguistic information and verbal communication with others has been validated widely in research and empirical evidence.[2,4-8]

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*Consultant, Early Childhood Education for the Handicapped, Minnesota Department of Education, St. Paul, Minnesota.

†Hearing Alert! Public Information Program: Early Detection of Hearing Impairment. Alexander Graham Bell Association for the Deaf, 1537 35 St. N.W., Washington, D.C. 20007.

The Law (Amendment to M.S. 1965, Section 120.17, Subdivision I): Preschool Handicapped:

> "Every school district and unorganized territory may provide special instruction and services for handicapped children who have not attained school age."

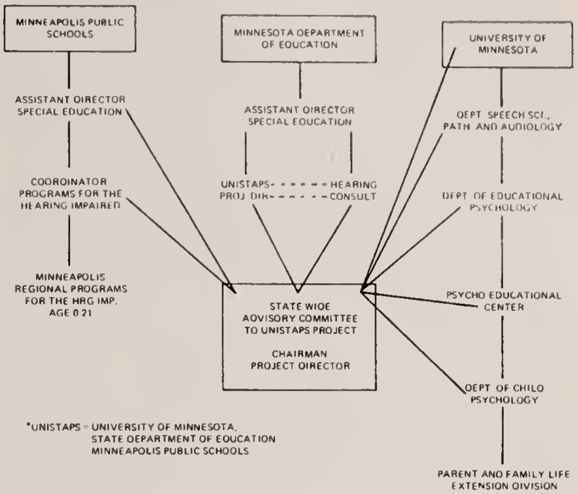
Historical Perspective

In 1967, in response to the rubella epidemic of 1964-65, the Minnesota legislature appropriated the sum of $120,000 for the biennium which would permit a local school district to provide a public school sponsored program for a preschool hearing impaired (deaf or hard of hearing) child and his parents. The line item appropriation was limited specifically to *hearing impaired* preschool children at that time.

The authorization included ½ unit of foundation aid and 60% reimbursement of salaries of essential personnel, supplies and equipment as for handicapped children of school age. In 1971, the appropriation was extended to include children with any disability identified in state statutes and added to the general budget. "Early intervention is cost effective," the evidence revealed. Several major factors contributed to the increasingly early support to young hearing impaired children and their families, which had their origins in the past two decades: (1) the state leadership provided by the Medical Director of Crippled Children Services, Dr. Mildred Norval, through provision of hearing and vision field clinics, pilot preschool education programs involving parents in the early 1960's, extensive inservice training of field nurses in the characteristics of young children suspected of severe hearing loss, and regional audiologists based in regional direct service educational programs (2) annual preschool parent institutes, the work of Dr. Frank Lassman, Professor of Otolaryngology and Speech, University of Minnesota, which ran from 1953 to the middle 1960's and offered a program of lectures, demonstration teaching and small group discussions (3) the vigorous activities of the Minnesota Department of Health and Minnesota Medical Association, each of which sponsors a preschool vision and hearing screening program heavily involving volunteers but coordinated to prevent overlap and duplication of efforts (4) the systematic routing of copies of audiological evaluations of young children from both the Audiology Clinic, University of Minnesota and Crippled Children Services to the state consultant for the hearing impaired, Minnesota Department of Education; the child's school district of residence; director of special education; special education regional consultant; the physician initiating the referral; and the child's parents.

It should be noted, parenthetically, that the same deficits in the system which were identified in earlier years are still "missing links" in the present system of screening detection, diagnosis, and referral for public school educational intervention. There is still the critical need for establishment of a statewide program of hearing testing services for infants judged to be "at risk" or "high risk" at birth or soon after. This must include referrals for medical, otological, and audiological screening and follow-up to insure the child and family have been linked to a formal educational program. A central registry and uniform data collection system, and new program funding sources are also required.

In 1968, the State Board of Education approved the *Educational Guidelines: A Family Oriented Preschool Program for Hearing Impaired Children in Minnesota* which represented the efforts of a consortium of representatives from major consumer, provider agencies and teacher training institutions relating actively to deafness; the State Department of Education hosted the meetings. Several innovative features in the *Guidelines* seem worth noting: (1) The term *preschool* is interpreted to cover the span of years beginning at birth or as soon as the diagnosis of hearing loss is established, to age four when mandatory school district responsibility begins. (2) The center of learning for the young child is considered to be his home, where spontaneous speechreading (lip reading), use of residual hearing and speech receive their maximum encouragement. (3) Parent counseling and parent guidance are integral components of the young child's educational program. (4) The integration of a hearing impaired child in a private community nursery, day care or Head Start program is considered preferential to a self-contained classroom where children would reinforce each other's silences and gesture language. (5) A district can formally contract with a private community nursery school for placement of a hearing impaired child and agreement to pay the tuition for his enrollment, thus becoming eligible for 65% state special education aid in reimbursement of the tuition paid by the local education agency, provided the teacher holds appropriate certification from the Minnesota Department of Education.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PSYCHO EDUCATIONAL CENTER
DEPT OF CHILD PSYCHOLOGY
PARENT AND FAMILY LIFE EXTENSION DIVISION

*UNISTAPS = UNIVERSITY OF MINNESOTA,
STATE DEPARTMENT OF EDUCATION
MINNEAPOLIS PUBLIC SCHOOLS

Figure—UNISTAPS* exemplary preschool program for hearing-impaired children, 0-4, and their families.

The UNISTAPS Project:* Minnesota Department of Education

A Family Oriented Program for Hearing Impaired Children, Birth to Four Years of Age

Tapping the Resources of the First Chance Network

In 1969, when Congress passed the Handicapped Children's Early Education Assistance Act (currently P.L.91-230, Title VI, Part C, Section 623) the Special Education laws and assurances were such that the State Department of Education in Minnesota, Special Education Section became one of the first 19 grantees in the country to develop a model demonstration program for preschool handicapped children. The child/family population was restricted to children with the single disability of hearing loss in order to mesh federal funds with existing parameters of eligibility for preschool special education state aids in Minnesota. The author resigned her position as State Consultant, Program for the Hearing Impaired to assume the position as UNISTAPS Project Director and thus remained a formal member of the Special Education Section. Currently, there are 175 model† demonstration programs, primarily with "mixed" populations, in the First Chance network administered by the Bureau of Education for the Handicapped, U.S. Office of Education.

The acronym UNISTAPS is not exactly a household word! However, it does highlight the diverse roles of the three participating agencies: UNIversity of Minnesota; STAte Department of Education; Minneapolis Public Schools (laboratory program) in developing a systems approach to public school sponsored early educational intervention for preschool hearing impaired children. The cooperative, consultative, coordinating nature of the relationship of these agencies has been carefully assured through (1) Advisory Committee membership (2) State Department of Education inservice training efforts and (3) the laboratory program (Minneapolis Public Schools) operations.‡

Nearly 200 hearing impaired children, 0-4, and their parents have been enrolled in the regional infant preschool program in the Minneapolis public schools, which has also served as the UNISTAPS laboratory during the past six years of federal funding. In 1973-74, the grant was extended to add a vision component serving 18 identified blind children and multihandicapped with vision impairment who resided within the Minneapolis city limits. The fifth year of funding by the Bureau of Education for the Handicapped also marked two additional innovations: the salaries of the *parent advisors/teachers* (N.B. this is their title in full) in the hearing impaired program were paid by local district and special education state aids and an Office of Child Development/UNISTAPS Collaborative Project was initiated to address to children with special needs in Head Start programs through joint planning and programming with directors of special education in Minnesota.

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*In 1975 the UNISTAPS Project was one of the first seven approved by the U.S. Office of Education Dissemination Review Panel for National replication and dissemination from among 175 operational programs in the United States funded under the Handicapped Children's Early Education Program. (P.L.91-230, Title VI C, Section 623).

†The term "model" is not to be equated with "exemplary" but should be examined as a way to intervene in the life of a young handicapped child and his family by enrollment in a program which has internal consistency (goals, objectives, activities, evaluation plan for improvement, not proof of the value of the model).

‡In November, 1972 ABT Associates, Inc. entered into a third party agreement to implement a "Project to Assess and Document Exemplary Programs for the Handicapped" for the National Institute of Education and the U.S. Office of Education, BEH. Seven of the existing 119 operational programs in the Handicapped Children's Early Education Program were detailed in Volume III of Exemplary Programs for the Handicapped. Early Childhood Education (Case Studies). The UNISTAPS Project was one: "a notable feature being its family involvement program."

The 1974-75 academic year brought additional expansion of the original population of hearing impaired children to include educational and coordinating services for Minneapolis preschool children who are severely handicapped (sensory deficits; physically handicapped; mentally retarded), on an experimental limited-enrollment basis. Following enrollment in the diagnostic-prescriptive nursery, a child may either be referred to a community sponsored special education program or enrolled in a direct service program at the Special Education Preschool Center.

Preschool State Guidelines

In December, 1974 the State Board of Education approved the *State Guidelines: Preschool Educational Programs for the Handicapped,* a major UNISTAPS Project objective during a four-year period of conceptualization and writing with the assistance of a multidisciplinary team. The laboratory program is being used to test the efficacy of the *Guidelines* through orderly implementation as a service model.

The basic premise of early intervention for handicapped children is that the local education agency, the public school, is a case finder (through the mandatory census), case manager and in many instances the coordinator of educational services in partnership with parents and the health care system.[10] "The multiplicity of causal factors relating to the handicapping condition(s) in a young child mandates consideration of (1) multi-agency involvement (health, education and welfare (2) a multidisciplinary team of specialists to serve the child and parents (3) cooperation and coordination among the involved institutions by individuals responsible for major decisions concerning the child and his family."

A Comprehensive Program for the Hearing Impaired Child 0-4/5 years and his Family

Following medical, psychological and audiological evaluation of each child through agency coordination, and perceptual-motor evaluation on referral, a family is enrolled and individual visits scheduled at the Home Living Center currently located at 830 N.E. Second Street, Minneapolis (formerly St. Anthony de Padua). Classrooms have been remodeled into a more home-like setting in order to permit the natural process of learning to listen(child) and learning to model and expand the child's primitive attempts at self expression(parent) through the relaxed, familiar parent-child times of interaction connected with a toddler's eating, playing, and seeking assistance from the adults in his immediate environment.

The focus is on the dynamic use of residual hearing incorporated into a child's every walking hour. During individual teaching sessions, a parent adviser gradually moves each parent from a passive role of observer to the lead role in offering short, useful sentences about the child's activities as they occur. The primary goal is *comprehension* of daily conversation related to child-initiated overtures to his toys and family, where the situation conveys meaning. At the same time parental guidance includes the development of competence in encouraging voice games and vocal play along with well-inflected conversation which helps a child to recognize and monitor the sounds he makes as a prelude to "chatter" and later, short sentences.

Since words and English syntax must be the child's "mother tongue" or native language, these can best be presented in a natural oral, rhythmic way to a young child who has established full time hearing aid usage. Sign language is not considered appropriate initially since the overwhelming majority of parents have normal hearing and in learning to become fluent in the use of one of the various forms of sign language, are unable to sustain the normal rate, rhythm and inflectional patterns of speech from which the young child receives his first linguistic information. Furthermore, a young child soon learns whether the signed word or spoken word is reinforced, with behavior in the desired direction. When a deaf parent is enrolled, an oral or manual interpreter is provided to insure active participation by parents in individual and group guidance sessions.

Major Services to Parents and Children

The comprehensive program components[13,14,15] offered by a multidisciplinary team include:

- parent counseling and guidance (individual, group); parent education (affective and instructional domains)
- nursery school experience with hearing children
- mother-child nursery (selected families)
- individual teaching (supplement to integrated nursery)
- home visitation (family or home living center)
- site visitation, community nursery school serving hearing impaired children
- inservice training, regular nursery school staff

The team members include: audiologist, social worker, early childhood education specialist, parent advisers (teachers of the deaf), occupational therapist and visiting support specialists (psychologist; family life specialist).

Laboratory Program Results

A variety of educational options have been provided for hearing impaired children at age 4 (minimum age, mandatory school district responsibility): (1) continuation in the integrated nursery school or day care center with supplemental acoustic instruction (2) placement in a self-contained class (3) half-day placement in a regular kindergarten with a supplemental half day in a self-contained class.

Changes Over Time

An examination of data relating to children enrolled in 1968-69 and newcomers in 1974 (fall) reveals the following information: Over a five year period of time (1969-1974) the median age of diagnosis of hearing loss for all enrollees has dropped from 36 months to 26. In the instance of children with profound hearing loss (91 db +) the change was from 24 months to 10 months.*

The median age of enrollment for all children dropped from 35 to 30 months in the same period. The age of enrollment for the 91 db + group (deaf by audiogram) dropped from 36 months to a median of 18 months.

Where Are the Infant/Preschool Program "Graduates" Placed?

Children may or may not have developed an auditorially based communication system following early identification, full time hearing aid usage and parental support when they have reached the primary grades. 80% of the infant/preschool children enrolled in 1968-1969 had a severe or profound hearing loss (71 db +). Their placements vary, with 56% being found in regular classes on a full day (50%) or partial day basis (6%).

Children who are candidates for a self-contained program may continue in an auditory-oral program or be placed in a classroom where the method of instruction is total communication (the addition of one of the forms of sign language and fingerspelling in addition to speech).

Research Findings: Integrated Children

Longitudinal and cross-sectional data, 1972-75, on 11 children with severe and profound hearing losses who are integrated in regular classes among 277 hearing classmates in nine school districts including Minneapolis, illustrate their assimilation in grades 3, 4, 5. Examination of the social status of the group as well as supporting evidence from direct behavioral observation and achievement skills data indicates no significant differences between the hearing impaired group (hearing loss ranging from 75-110 db, pure tone average in the speech range) and a random sample of normal hearing classmates.[11,12]

Outreach and Dissemination

In addition to more than 2,000 visitors to the Minneapolis Infant/Preschool Program in the past six years, a vigorous program of inservice training has been offered by the Special Education Section, Minnesota Department of Education in the form of special study institutes; state conferences for parents; contracted college courses and technical assistance to public school direct service preschool programs.

Currently, an additional member has been added to the UNISTAPS staff at the State Department of Education who has the title Coordinator: Major State Provider/Consumer Agencies.† The goal is mutual exploration of current services and resources which are integral to early childhood programs for the handicapped in an attempt to develop an information exchange system required in order to implement comprehensive early childhood education programs and services for handicapped children.

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*The interval between diagnosis and enrollment ranges from one week to one year, the latter primarily due to impending surgical procedures. The increase in median ages of children with 41-70 db loss (unaided) reflects increased numbers of hard of hearing children previously not identified until kindergarten or first grade who are now entering at the preschool level.

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Summary

The activities developed under UNISTAPS aegis have been both participatory and stimulatory.[16] In addition to provision of a direct service training program for certain hearing impaired children in the Minneapolis public schools which also serves as a model for site visitation, the Project goals relate to a systems approach to stimulate replication in whole or in part through local school district application of the *State Guidelines: Preschool Educational Programs for the Handicapped in Minnesota.*

In sparsely populated areas, certain speech clinicians function as regional specialists offering parent guidance as well as auditory and linguistic stimulation to newly identified hearing impaired preschoolers and their families. They have attended UNISTAPS sponsored workshops for professional growth experiences with the preprimary hearing impaired child since 1969. Their direct service and monitoring roles are arranged through contact with the infant's district of residence and the clinician's employing district.

Thus the "ripple effect" is noted, through increased interface among Directors of Special Education or Special Education Regional Consultants and Head Start Mediator team members for the purpose of communal and comprehensive services to preschool children with special needs.

For every right . . . to a federal grant and its monetary award—there is an awesome responsibility for each involved staff or Advisory Committee member. It is believed by many observers in Minnesota that in this instance federal "seed money" fell on fertile soil nourished by the actions of the Minnesota legislature and its concerned citizens.

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Mayo Clinic

The Mayo Clinic has announced the retirements of Dr. Norman Christensen, an internist; Dr. Lloyd Harris, a pediatrician; and Dr. Wallace Merritt, a rheumatologist.

Addiction

The Routine Administration of the Michigan Alcoholic Screening Test to Ambulatory Patients

ROBERT B. BREITENBUCHER, M.D.*

A Self-administered version of the Michigan Alcoholism screening test (MAST) was given routinely to 252 ambulatory patients who were undergoing a complete examination. In 17% of these patients the MAST was the only readily available means by which alcoholism could be suspected. Forty-two percent of all the patients were alcoholic as identified by the MAST and/or other parameters. There was a 10% incidence of false negative MAST scores. The MAST as described is a practical screening test for alcoholism which can be rapidly and easily given to ambulatory patients. *The apparent failure of physicians to deal with alcoholism is an obstacle to the discovery and treatment of alcoholics in early stages.*

THERE ARE A LARGE number of alcoholics seen at this hospital. In addition there are large numbers of alcoholics attending our outpatient clinics who are unrecognized. The recognition of alcoholism in early stages is difficult because of characteristic denial patterns manifested by the alcoholic.[1,2] The average physician finds dealing with alcoholics unrewarding and frustrating and views the problem of alcoholism with an attitude of hopelessness. The time required to take adequate alcohol histories is not a practical matter in most physicians' practices.[3] The problem of alcoholism is not as hopeless as many assume.[4] It is important to identify alcoholics before the devastating social and physical consequencies of end-stage alcoholism are present. A method which is practical and simple enough to serve as a routine screen for alcoholism, is the Michigan Alcoholic Screening Test (MAST). [5,6] The use of the MAST as a self-administered procedure given to all patients in the General Medicine Ambulatory Care Clinic as a part of a complete examination is the subject of this report.

Methods

The 24 MAST questions are on individual cards. The patient is instructed to answer the questions by placing the cards in boxes clearly marked "yes" or "no." The cards are coded to identify the cards indicative of the alcoholic response. There are marks on the cards to confuse anyone who might be inclined to figure out the system. The time required to explain the test and to score the test is about five minutes. Alcoholic responses are weighted according to Selzer's original method. The value of the score is coded on each card. The person scoring the test adds up the total points to obtain the total MAST score. Another simple code records which questions the patient responded positively to. This information is helpful for subsequent interviews with the patient. According to studies by Selzer[5,6], a score of four is suspicious of alcoholism and a score of five or more is presumptive of alcoholism. Scores of zero to three are considered negative. We used the questions as originally stated by Selzer. It became apparent to us during this study that a few of the questions were subject to misinterpretation and we have revised them. The questions as we now state them are listed in Table 1.

All patients undergoing a complete examination in the General Medicine Ambulatory Care Clinic are subjected to preliminary studies before receiving a final complete examination by a physician. The MAST test was administered to patients at the time of the preliminary examination. Except for some records which were unavailable and a few who refused to take the test, this report is based upon the records of all patients presenting for a complete examination between August 1, 1974, and January 7, 1975. Review of records for purposes of this study was accomplished by reviewing all available outpatient, in-

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See editorial, page 395.

patient, and Emergency Room records of patients who had done the MAST.

Results

Two hundred fifty-two records were reviewed. There were 137 males (54%) and 115 females (46%) ages 16 to 83 years. There were 132 patients (52%) who had MAST scores of 0 to 3; 16 had a score of 4; 104 (42%) had scores of five or more. The distribution of scores is shown in Table 2.

There were 70 patients in whom alcoholism could be suspected from the records other than that afforded by the MAST. Eighty-three percent of this group were males. The parameters upon which alcoholism was suspected included Emergency Room visits for injury where drunkenness was recorded, visits to the Emergency Room under police escort, at which time blood alcohols of 0.3% or greater were found, a diagnosis of alcoholism made previously by professionals in contact with the patient, presence of liver and neurological complications of alcoholism, and a history of alcoholic treatment either in a detoxification unit or other treatment centers.

MAST scores were five or greater in sixty

TABLE 1
MAST Questions

	Score	Positive Answer
1. Do you feel you are a normal drinker? (By normal we mean you drink less than or as much as most other people.)	2	No
2. Have you ever awakened the morning after some drinking the night before and found that you could not remember a part of the evening before?	2	Yes
3. Does your wife, husband, a parent, or other near relative ever worry or complain about your drinking?	1	Yes
4. Can you stop drinking without a struggle after one or two drinks?	2	No
5. Do you ever feel guilty about your drinking?	1	Yes
6. Do your friends or relatives think you are a normal drinker?	2	No
7. Are you always able to stop drinking when you want to?	2	No
8. Have you ever attended a meeting of Alcoholics Anonymous (AA) for yourself?	5	Yes
9. Have you gotten into fights when drinking?	1	Yes
10. Has drinking ever created problems between you and your wife, husband, a parent, or other near relative?	2	Yes
11. Has your wife, husband, a parent, or other near relative ever gone to anyone for help about your drinking?	2	Yes
12. Have you ever lost friends or girlfriends/boyfriends because of drinking?	2	Yes
13. Have you ever gotten into trouble at work because of drinking?	2	Yes
14. Have you ever lost a job because of drinking?	2	Yes
15. Have you ever neglected your obligations, your family or your work for two or more days in a row because you were drinking?	2	Yes
16. Do you drink before noon fairly often?	1	Yes
17. Have you ever been told you have liver trouble? Cirrhosis?	2	Yes
18. Have you ever had delirium (DTs), severe shaking, heard voices or seen things that weren't there after heavy drinking?	5	Yes
19. Have you ever gone to anyone for help about your drinking?	5	Yes
20. Have you ever been in a hospital because of drinking?	5	Yes
21. Have you ever been a patient in a psychiatric hospital or on a psychiatric ward of a general hospital where drinking was part of the problem?	2	YES
22. Have you ever been seen at a psychiatric or mental health clinic, or gone to a doctor, social worker, or clergyman for help with an emotional problem in which drinking had played a part?	2	Yes
23. Have you ever been arrested, even for a few hours, because of drunk behavior?	2	Yes
24. Have you ever been arrested for drunken driving, driving while intoxicated, or driving under the influence of alcoholic beverage?	2	Yes

TABLE 2
MAST Scores 252 Patients

Score	0-3	4	5	6	7-20	21-30	>30
No. (%)	137 (52%)	16 (6%)	13 (5%)	9 (4%)	38 (15%)	16 (6%)	28 (11%)

(86%) of these patients; two had a score of four; and eight had scores of zero to three. The average score of those who scored five or greater in this group was 27.8. The highest scores were found in this group of patients and ranged up to 52. There were 57 patients (23%) in whom alcoholism could be suspected, without resorting to an alcoholic interview, only on the basis of the MAST. Fourteen (6%) had scores of 4; and 43 (17%) had scores of five or greater, ranging from five to 40 and averaging 11.9. The male predominance was not as great in this group of patients. There were six males and eight females who scored four, and 26 males and 17 females in the group that scored 5 or more.

Physician awareness of alcoholism in these patients was judged by the appearance of alcoholism on the problem list or some mention of alcoholism or chemical dependency in the notes made by the physician who examined the patient either at the time of his complete examination or on some subsequent visit. In the group of 70 where alcoholism could be suspected on the basis of parameters other than MAST and, of course, including the MAST, *only 32 were recognized by the physician* as far as could be determined by any notation on the records. In 27 there was no evidence of awareness of alcoholism by the examining physician recorded on the chart. Eleven patients did not return for examination after the preliminary studies and thus were not seen by a physician.

Of the 59 patients who were seen by a physician, in only 21 was there any indication that the physician had made some effort to deal with alcoholism or indicated awareness of the fact that others were dealing with the problem. In some cases the patient was in treatment programs prior to the examination. In 36 cases in this group, however, there was no evidence from the records that alcoholism was being dealt with at all by anyone.

In the group of patients who did not have any evidence of suspicion of alcoholism to be found on the records other than the MAST scores of five or greater, in only five of these did this fact appear to be recognized as a problem. There was no evidence of recognition in 27. The nursing staff did not even record the MAST on the chart on eight and three patients did not return for a physician examination in this group. There was no evidence of recognition of a possible problem in the 14 who scored four. Of the 46 patients who had these MAST results recorded, in only one instance did the physician make any comment as to any effort made to seek confirmation or in any way deal with the question of alcoholism.

Comment

Defining alcoholism is a difficult task[7] and there is not unanimity of opinion in this regard. There is a danger in making the definition too objective and too stringent, thus risking nondiagnosis of alcoholics who if discovered might be helped to a better life for themselves and those around them. In general, it seems that a functional definition as used by Keller[8] is a practical clinical guide: "Alcoholism is a chronic disease manifested by repeated implicative drinking so as to cause injury to the drinker's health or his social or economic functioning." The 24 questions of the MAST test devised by Selzer[5,6] are designed to try to elucidate the important deleterious functional aspects of alcoholism and, hence, determine the probability of alcoholism. A number of studies attest to the utility and effectiveness of the MAST or modifications of it as a screening device for the detection of alcoholism in inpatient settings involving various types of clinical practice.[9-14] This study was designed to test the practicality and effectiveness of administering the MAST routinely to patients seeking complete examinations in a General Medicine Ambulatory Care Clinic. The Clinic is part of a metropolitan county hospital which has to deal with an inordinate number of alcoholics in the end-stages of their disease. It is important to emphasize that alcoholism is not confined to county hospitals and medical centers. A substantial number of alcoholics may be found in any medical practice. I would further emphasize that the method and application of the MAST as used in this Clinic is applicable to any ambulatory practice and, as judged by the results of this study, will yield evidence of more pathology (alcoholism) than probably any other routine test that we do. Review of records to try to establish the probability of alcoholism by parameters other than the MAST was done for two reasons. One was to determine how often alcoholism could be suspected on the basis of the MAST that could not be readily suspected by other parameters not including an alcohol interview. The other was to seek some means of validation of the MAST itself in terms of our own experience. It is not surprising that the MAST scores in the group of patients who had evidence of alcoholism by other parameters were quite high. The average score of those who were positive in this group was over twice as high as the scores in the group where the MAST was the only indication. On the other hand, there were two patients who had borderline scores of four and eight patients who scored in the zero to three range. Three reasons were apparent for this failure of the MAST to detect some obvious alcoholics. One was the obvious reason that the patient was simply able to lie well enough to confound the test. Another reason was that there was some evidence that some "reformed" alcoholics may be reporting present experience and are choosing to ignore past experiences. Finally, there is the unusual "controlled alcoholic" who is able to tolerate large amounts of alcohol without experiencing the behavioral problems that most others do.

The real importance of the MAST is its ability to raise the suspicion of alcoholism in patients not readily discoverable by the usual examination routine of clinical medical practice. Fourteen (6%) had scores of 4 and forty-three (17%) had scores of 5 or more. If we conservatively assume an accuracy of 75% in the diagnosis of actual alcoholism in patients with MAST scores in this range of four or greater, this would mean that we are able to diagnose the early stages of alcoholism in about 17% of our patients. I can think of no other diagnostic procedures that we use daily which will lead us to discovery of disease in 17% of those examined. The treatment of alcoholism does not deserve the pessimism with which most physicians tend to look upon it.[4] Alcoholism is a major disease in our society. The discovery and treatment of alcoholism in present day society rivals the challenge of discovery and treatment of tuberculosis in the past. Discovery and treatment of early stage alcoholism is truly an exercise in preventive medicine.

The MAST per se cannot be considered a definitive diagnostic instrument. It is a screening device. Confirmation of alcoholism should be obtained by probing, sometimes confrontive type of interview.[3] We tried to establish a routine whereby the physician performing the examination would ask for an alcohol counselor to come to the clinic to interview his patient with a positive MAST score, preferably conjointly with a physician. It became apparent that *inaction by the physicians* in charge of these patients constituted a roadblock to dealing with the alcoholic as revealed by this study. Although we feel that it is ideal and sometimes essential to have the physician in active participation in dealing with the alcoholic, we have found it necessary to establish a routine of discovery and referral for treatment now which is not dependent upon physicians. This system is currently under assessment but seems to be working better. We are continuing to try to encourage our physicians to become more actively involved, but in the meanwhile in the interest of effectively dealing with alcoholics we are not unduly dependent upon the physician.

Our physicians are not unique in their apparent lack of interest in dealing with alcoholism.[16,17] Dealing with alcoholism assumes a low priority for most physicians. Alcoholics are often manipulatory, devious, and frustrating patients to deal with. As previously mentioned, the techniques of interview are not familiar ones for physicians and tend to consume more time than a physician is willing to spend in an endeavor which he thinks is probably hopeless anyway. There are many demands on a physician's time so it is not hard to put dealing with alcoholics rather low on the list of priorities. The prospects for alcoholics under present-day management is more hopeful than has previously been the case. Help in dealing with alcoholics is becoming more readily available from professionals in this field. At present, in many areas, it is just a question of the physician and his patient participating in what is readily available for the discovery and treatment of alcoholism. The MAST is a valuable, simple, routine diagnostic instrument which should be used for the discovery of alcoholism in any practice which devotes itself to the comprehensive care of the patient.

Summary

A self-administered Michigan alcohol screening test was used in our General Medicine Ambulatory Care Clinic. It is an effective, simple screening method for alcoholism which can be easily applied for any ambulatory care practice. A major problem in effectively implementing therapeu-

tic modalities for alcoholism *is a lack of interest and involvement of physicians in the problem of alcoholism.*

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Mental Health

Erosion of Indian Mental Health in Cities

JOSEPH WESTERMEYER, M.D., Ph.D.*

Over the last two decades Indians have increasingly migrated from reservations to large cities. Once away from home, Indian people encounter increased mental health problems. Psychologically and socially, Indian people are immigrants in their forefathers' land. Their personal and social adjustments to city life are fully as difficult as those experienced by immigrants from other continents. Indeed, in the light of historical relationships between Indian people and the majority society, the adjustment demanded of urban Indians is perhaps greater than that required of many other groups.

THIS PAPER GROWS out of clinical experience, mental health consultation, and research activities with urban Indian people (mostly Chippewa and Sioux) in the Twin Cities. During that time collaboration with Indian people has included the following: clinical work with 300 urban Indian patients and family members; board membership with two urban halfway houses for Indian alcoholics; consultant to two urban programs for Indian health; and research on majority institutions vis-a-vis Indians, Indian alcoholism, and violent death.[1-8] This paper comprises a synthesis of these experiences, with implications for mental health planning by and for Indian people.

The Problem

Indian people have much the same kinds of problems in cities that they have on reservations. However, some of these problems occur with greater frequency in the city than on the reservation. These include, for example, child abuse, state guardianship of Indian children, and the consignment of Indian adolescents to reform schools. Other problems are no more frequent in the city, but—for reasons to be elaborated upon—are more incapacitating for the urban Indian than for the Indian living on a reservation. These include marital breakdown and termination of parental rights; alcoholism and drug abuse among all ages; runaways, delinquency, school drop-out, and unwanted pregnancy among young people; and suicide attempts.

A major point regarding Indian strengths should be emphasized. In other cultural groups, these problems which are now common among Indian people are usually prevalent among lower socioeconomic classes, the unemployed, the poorly educated, and those with little political power. When it comes to psychiatric disorders which are *not* strongly affected by social and cultural factors—such as severe mental retardation, major mental illness, incapacitating neurosis and senility—Indian people have rates that are comparable to (or sometimes slightly lower than) non-Indian people. This suggests that reservoirs of strength exist among Indian people which allow them to cope with overwhelming social and environmental stresses. The momentous problems listed below, then, are not viewed as indications of psychological infirmity inherent among Indian people, but as evidence of the rapacious milieu in which they must live and the relative absence of social support systems (i.e. family, friends, health services, private agencies) which we all require for existence in today's complex urban society.

Migration and Alienation

Urban Indian as Immigrant

Twenty years ago at the end of World War II there were but a few hundred Indian people in the Twin City area. Now they number twelve to fifteen thousand, most of whom have come from reservations to the city in the last decade or two. Only one Indian patient out of 300 known to the author was born in the Twin Cities; the remainder were born on or near reservations.

Indian people coming to the city can be considered immigrants within their own country in the same sense that people from Europe, Africa, and Asia are immigrants to the United States.

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See editorial, page 395.

Indian people encounter a physical environment, social organizations, interpersonal behaviors, attitudes, values, and sometimes even language that are foreign to what they have known. Indeed, many values and behaviors prevalent in the city are the opposite of what they were taught on the reservation. These include accumulating material goods rather than sharing them, competing with others rather than collaborating with them, resolving group problems by majority rule rather than by consensus.

Indian people often find themselves accepting what their non-Indian neighbors question, and questioning what the others accept. As they become accustomed to city living, they discover that they are acting like two people instead of one: like a White person at work or among their neighbors and like an Indian person at home or among relatives. Consequently, their behavior and their values may come into conflict, with resulting confusion over what is right and wrong and over the propriety of their thoughts and actions.

The City as a Hostile Environment

The city not only imposes stresses on its Indian immigrants; it also undermines their traditional resources. The urban Indian "ghetto" is not merely a transplanted reservation. It is not located on the land with which they have come to identify themselves, nor is there a tribal council and tribal law. Indians in cities do not retain their full status as citizens with special treaty privileges.

Perhaps most detrimental is the fact that the Indian "ghetto" is not really a true ghetto composed of one homogeneous group. Rather it is a racial and ethnic admixture of people who often share one limited characteristic: poverty. Thus, city Indians do not live solely among Indian people as they do on the reservation, but are among Whites, Blacks, and Spanish speaking peoples. In such an ethnic admixture, many of their traditional beliefs and values are further undermined—especially those which possessed survival value on the reservation (such as the "sharing" ethic), but are often not advantageous in the city.

Separated by distance from the reservation and even from their relatives who reside in the same city, the nuclear family is thrown more on its own resources. This weakens the single greatest social asset of the average reservation Indian: the extended kin group. At the same time the urban Indian—whether from inexperience with urban living or poverty or both—does not innately employ the social resources which the majority society has evolved to take the place of kinship. While Indian people have begun to develop their own non-kin resources (as did Lutherans, Jews, and Catholics before them), these resources are still too small or too poor to help many Indian people who need assistance.

Indian-Majority Antagonism

The Indian immigrant to the city has a further disadvantage that did not affect the European immigrant: a distrust of White people and majority institutions. Oral tradition and written history[9-12] teaches the Indian that the White people are the enemy. They originally attacked Indian groups to take land. Land which was not confiscated by military might was taken by civilian deceit.

Conquest was followed by a widespread economic dependency; the latter has further exacerbated the mutual mistrust between Indian and non-Indian people rather than ameliorated it. Even some Indian and White idioms reflect the prevailing problems with inter-cultural communication (e.g. "Indian giver" among Whites, "acting like a White man" among Indians). As a result urban Indians have another dilemma to face: they must often depend on those whom history, tradition, and experience teaches them they should not trust. And of course, the dependency status inevitably results in a socio-economic status inferior to majority people.

Economic Disadvantages

Finally, Indian people are unprepared by child raising practices, education, and adult role models for economic survival in the cities. One can drive a school bus or cut pulp wood or hunt on a reservation with a grade school education, but good jobs are not available to city dwellers without training past high school. Indian immigrants to the city are even at a marked disadvantage compared to immigrants from other nations who come here with graduate degrees and professional credentials to join the affluent among us. Even foreign nationals without such degrees usually have urban relatives who can guarantee employment for them.

Alienation of Indian People and Majority Institutions

Little collaborative planning occurs between Indian people and majority institutions. Logically this is unexpected, since Indian people flood certain majority institutions out of all proportion to their small numbers in the population. Hundreds of welfare workers, child protection workers, workhouse guards, reform school counselors, police, jailers, judges, truant officers, homicide detectives and others have as a major part of their daily work to arrest, jail, judge, house, pick up, drop off, place on relief, and otherwise handle thousands of Indian people. It would seem fiscally less expensive, and certainly more humanitarian for Indians and social institutions to begin outreach programs stressing early case finding, crisis intervention, and problem resolution rather than problem maintenance.

But it does not happen. For prevention and outreach programs to be effective, there must be a transfer of money, authority, and responsibility into Indian hands. However, the history of our society, its various levels of government, and its various agencies over the last century indicate that such sharing of power over Indian lives is an abhorrent thing for our governmental agencies, missionary groups, schools, law enforcement groups, health planners, and others.

Indian people collude in maintaining the *status quo*. Among many Indian leaders there is a reluctance to talk about problems of child neglect, child abuse, inadequate parenting, delinquency, drug abuse, alcoholism, marital breakdown, and violent death among their own people. Until these issues can be courageously addressed by Indian leaders and brought to the awareness of both Indian and non-Indian citizens, little change for the better can be expected.

Discussion

It would indeed be extraordinary if Indian people were to come to multi-racial, multi-ethnic cities and not experience a marked increase in mental health problems of some kinds. Among all immigrant groups thus far studied, first generation migrants experience high rates of severely incapacitating mental health problems. Even among European groups that become economically successful in the United States, identity problems and associated emotional disturbances have been noted to persist for a few generations following migration.[13-18] One can expect that Indian people, immigrants in their forefathers' land, will also encounter inordinate mental health problems for years and perhaps even for generations to come.

Currently Indian people with mental health problems rarely receive psychiatric care, marital counseling, or other rehabilitation. In cases where majority institutions do become involved, problems are frequently made worse rather than ameliorated. Urban Indians in crisis are commonly separated from home, family, job or school.

Greater involvement by Indian people, organizations and communities promises to reverse this trend.[4,19,20] More Indian families could be kept intact through crisis by temporary placement of Indian homemakers. Where placement of Indian children out of the home is necessary for a time, Indian foster homes and Indian group homes should be available. With adequate financial resources, Indian communities could place their own advocates, counselors, and attorneys in courts, hospitals, and agencies so that majority judges, social workers, and physicians would learn effective means of working with Indian people. Premarital and prenatal training courses could be offered by Indian churches and community centers. More Indian cultural enrichment courses, Indian counselors, Indian teacher's aides, and Indian run schools could be introduced into the educational system. Such directions would involve Indian people in the solution of their own community problems and would provide Indian role models for Indian children and adults in crisis.

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President's Letter

Homicide or Death?

As the law now is interpreted in Minnesota a physician who turns off the respirator on a patient whom the physician believes has experienced an irreversible cessation of spontaneous respiratory and circulatory function may face a charge of *homicide.*

Recent advances in medical technology and skills such as: respirators, closed cardiac massage, pacemakers, and defibrillators have saved countless numbers of lives and restored the health and meaningful existence for patients who would have almost certainly succumbed to their diseases just a few years ago. As a result of these significant clinical advances and beneficial effects on patients and their welfare, medical science has now developed the capability to reestablish and maintain vital functions by artificial means of support for prolonged and indeterminate periods of time in patients with massive irreversible brain damage. Thus cases of brain death—patients who are totally supported in a respirator with no clinical evidence of brain function—have become increasingly common in hospitals throughout the state of Minnesota and the United States.

In spite of the common occurrence of brain death and the well established acceptance of the concept of brain death by the medical profession, patients, families, and physicians are confronted with legal uncertainty and potential civil and/or criminal liability in these cases.

The most appropriate forum for discussion and changes in the law recognizing the concept of brain death would be the State Legislature.

Working toward this end, the Minnesota State Medical Association formed an Ad Hoc Committee on Death under the chairmanship of Dr. Ronald Cranford, a neurologist at the Hennepin County Medical Center. The committee, realizing that the AMA House of Delegates adopted a resolution in June of 1974 which recognized that permanent and irreversible cessation of function of the brain constitutes one of the various criteria which can be used in the medical diagnosis of death, probed all the ramifications of Death and Dying which we are all familiar with to find an initial solution. They proposed a model statute to the Council of the MSMA which was accepted. This past May it was introduced to the House of Delegates where it was amended and adopted. It will hopefully be introduced to the Minnesota Legislature in January 1977. The committee knew that the lower courts would not handle the problem, that nine states have statutes that legalized the concept of brain death and that the AMA and the ABA accepted the concept. The committee did not want to develop criteria, just the concept of brain death. Thus, it would not restrict future changes in medical criteria or retard further medical research, although there is a demand for uniform medical criteria which can be used to determine brain death.

The Ad Hoc Committee on Death of the Minnesota State Medical Association recommended that the concept of brain death should be legally recognized through the enactment of Model Statutory Legislation as amended and adopted by the House of Delegates. The proposed legislation reads as follows:

A person shall be pronounced dead if, in the opinion of a physician, based on current standards of medical practice, that person has experienced an irreversible cessation of spontaneous respiratory and circulatory function. In the event that artificial means of support preclude the determination that these functions have ceased, a person shall be pronounced dead if, in the opinion of a physician, based on current standards of medical practice, that person has suffered *an irreversible cessation of clinically determined total brain function.*

A non-partisan legislature should enact this statute in 1977, thus responding to a great and urgent social need.

Richard E. Anonsen, M.D.
President
Minnesota State Medical Association

Cover Photograph

"Flag of 1825 over Fort Snelling"

The Flag of the United States is the third oldest of the national standards of the world; older than the Union Jack of Great Britain or the Tricolor of France.

During the early days of the Revolutionary War a variety of flags were used by the different colonies and military commands. Prominent among these were the "Pine Tree" and "Rattlesnake" flags with various arrangements and mottoes.

In 1775 a committee of Congress with Benjamin Franklin at the head, decided upon the form for a new flag. This flag consisted of thirteen stripes, red and white, with the crosses of St. George and St. Andrew on a blue field in the union. This preceded the Declaration of Independence and indicated that the colonies had not wholly broken from the mother country. This flag was first unfurled by Washington, January 2, 1776. It was probably the flag raised by Paul Jones on his vessel and carried by the American fleet which sailed out of Philadelphia in February, 1776.

On June 14, 1777, Congress passed an act stating "That the Flag of the thirteen United States be thirteen stripes, alternate red and white, that the union be thirteen stars, white in a blue field, representing a new constellation." This was the birthday of the Flag as we now know it.

The new flag was probably displayed at the Battle of Bennington, Vermont, August 16, 1777. This flag remained the national standard until 1795. The first display of the Stars and Stripes by the Continental Army was when the Flag was hoisted over Fort Stanwix, New York, on August 3, 1777.

In the meantime Vermont and Kentucky had become states and on January 13, 1794, Congress voted that the Flag should have fifteen stripes and fifteen stars. This Flag remained in use for 23 years, and it was "The Star Spangled Banner" of which Francis Scott Key wrote in 1814.

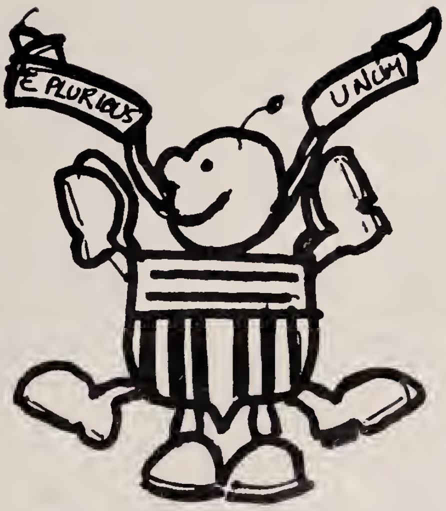
In April, 1818, Congress passed an act providing that the Flag have 13 horizontal stripes, alternate red and white, and the Union should display 20 stars, the number of states then in the Union. It also provided that on the admission of every new state to the Union a star should be added on the following July 4th.

The Flag on the cover of this issue of MINNESOTA MEDICINE dates back to 1825 and contains four more stars than the one flown in 1817 for states entering into the Union after that year, namely, Illinois, Alabama, Maine, and Missouri. The next state to enter the Union was Arkansas in 1836, and the last state was Hawaii in 1959.

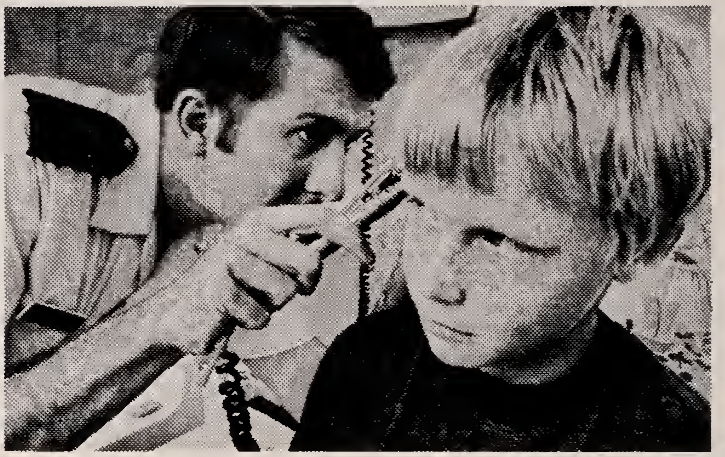
Editor's Notebook

bug in the belfry

boston massachusetts
well here i am
in the belfry
of the old north church
while my boss
the editor
is in boston
preparing for the future
i am going
to celebrate the past
after all
here is where
the action is
if you are bugs
about the bicentennial
from the light
shown here
paul revere and william
dawes along with
doc sam prescott
rode off
in all directions
to alert the colonists
to fight for the idea
that all men
are endowed
with certain
inalienable rights
among them
life
liberty
and the
pursuit of happiness
even to a bug like me
200 years later
those rights have
the right ring
they make me feel good
you might say
they are good
for my constitution
minny



p.s.: I have no hat because I a trying to look like a bald eagle.



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ontents—July, 1976

OVER PHOTOGRAPH—"1825 Flag over Fort Snelling" 440

RESIDENT'S LETTER—Homicide or Death?
Richard E. Anonsen, M.D., President 439

DITOR'S NOTEBOOK—bug in the belfry
minny 441

RIGINAL CONTRIBUTIONS

Hypernephroma—A Plea for Earlier Diagnosis
Dwenda Van Veldhuizen et al. 445
Parathyroid Adenoma Presenting as a "Cold Nodule" on Thyroid Scan
Robert S. Lund, M.D. and Rex B. Shafer, M.D. 448
Uterine Prolapse and Upper Urinary Tract Obstruction
T. A. Hildreth, M.D. et al. 450
Cerebellar Hemorrhage
Frederick M. Vincent, M.D. 453

DITORIALS

The Proud Profession
Reuben Berman, M.D., Editor Emeritus 463
Cerebellar Hemorrhage
Edward R. Laws, Jr., M.D. 464
Cold Thyroid Nodule
Stanley C. Von Drashek, M.D. 465
Tennis Elbow
Elmer R. Salovich, M.D. 465
National Cooperative Gallstone Study
Russell F. Hanson, M.D. and Johnson L. Thistle, M.D. 465

TTERS TO THE EDITOR

Provider Agreements
James Janecek, M.D. 468
Biting Insects
C. A. Frazier, M.D. 468

INNESOTA MEDICINE HONOR AWARDS 469

EDICAL LIBRARY—LATCH
Sherry A. Hargrave 477

ISTORY—Hessian Troops in the American Revolution
Rudolf Schmitz, Ph.D. 479

INNESOTA STATE MEDICAL ASSOCIATION—Annual Meeting
R. D. Semsch, M.D. 478

INICAL PATH CONFERENCE—Fatal Iron Poisoning in a Pregnant Female
Robert L. Strom, M.D. et al. 483

SMA HIGHLIGHTS—Division of Socio-Economic Affairs 492

RINATAL MORTALITY—The Changing Patterns of Perinatal
ortality at a Suburban Community Hospital
Sylvester J. Sanfilippo, M.D. 495

ISTORIC HOSPITALS—Bedside Medical Teaching Among the Arabs
Warren L. Kump, M.D. 502

OOK REPORTS 501

ASSIFIED ADVERTISEMENTS 503

DEX TO THE ADVERTISERS 506

Volume 59, 7
Pages 435-506

MINNESOTA
MEDICINE
REPRESENTS

Association of Neurologists of Minnesota

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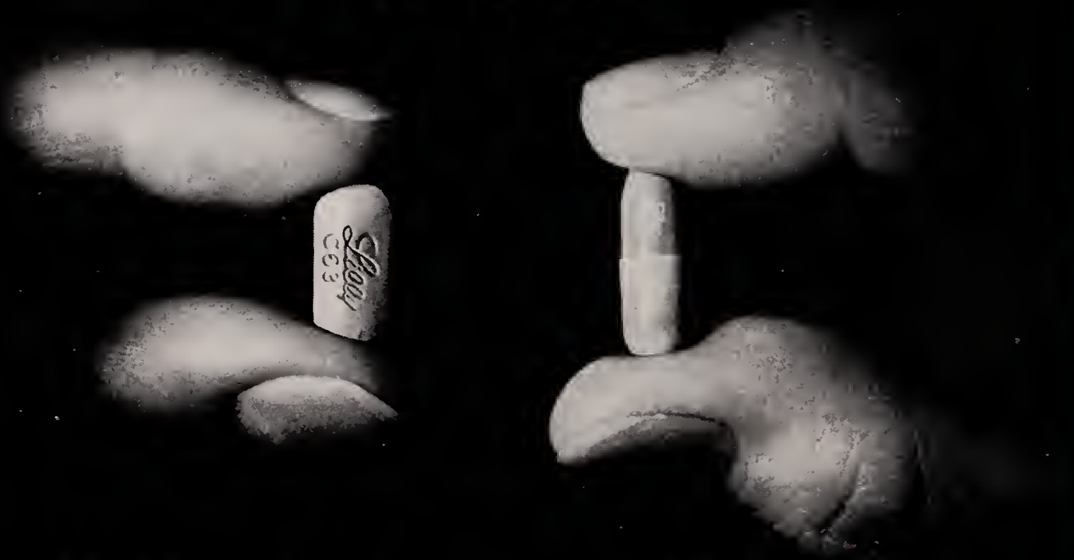

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Hypernephroma

A Plea for Earlier Diagnosis

DWENDA VAN VELDHUIZEN;* J. J. TIEDE, M.D.† and L. C. GILMAN, M.D.#

The cases of five patients with renal cell carcinoma which were diagnosed during a month period at the Willmar Medical Center are presented. A discussion is included of the presenting symptoms of this disease. It is suggested that although the diagnosis usually can be made before the appearance of the classic triad of symptoms (hematuria, mass, and pain) many patients continue to be seen only after systemic symptoms are present.

THE CASES OF five patients with renal cell carcinoma are presented. The five were seen during a one-month period at the Willmar Medical Center. Each underwent a nephrectomy and was apparently well two months later.

Case Reports

Case 1

A 61-year-old man was seen with a history of chills and dyspnea. Hb was 11.1 gm. %. Urinalysis showed 2-3 red blood cells/hpf. Serum iron was 27. Total iron binding capacity was 158. Intravenous pyelogram showed a mass in the lower pole of the right kidney, which was also visualized by arteriography. At surgery the tumor was 8 x 5 x 6 cm. and extended into perirenal fat.

Case 2

A 75-year-old woman presented with weakness, fatigue, insomnia, and anorexia. She had a firm, slightly enlarged liver. Hb was 7.4 gm. %. Serum iron was 14. Iron binding capacity was 176. Iron saturation was 8. Urinalysis showed 4-10 red blood cells. SGOT, alkaline phosphatase, and LDH were normal. Liver scan showed multiple defects. IVP revealed a 9 cm. mass in the lower pole of the right kidney. Arteriogram demonstrated a mass lesion (Figure 1). At surgery the mass extended into a calyx, although not into vessels. The right kidney was removed. Liver biopsy revealed cavernous hemangiomas.

Case 3

A 79-year-old male presented with a one day history of painless hematuria the week prior to admission. Urinalysis showed a packed field of red blood cells. Hb was 12.1 gm. %. IVP revealed a left renal mass, which was confirmed by arteriography. Left radical nephrectomy was performed. The tumor measured 7 x 8 x 7 cm. and had invaded the renal vein. Recovery was complicated by left ileo-femoral thrombophlebitis for which thrombectomy was done.

Case 4

A 64-year-old male had night sweats, fatigue, nocturia, headaches, and weight loss of 20 pounds during the six months prior to admission. Hb was 9.2 gm. %. Microscopic hematuria and a varicocele were present. IVP was non-diagnostic but suggested an indefinite left renal outline (Figure 2). Renal arteriography indicated a left renal tumor mass (Figure 3). The left kidney was excised.

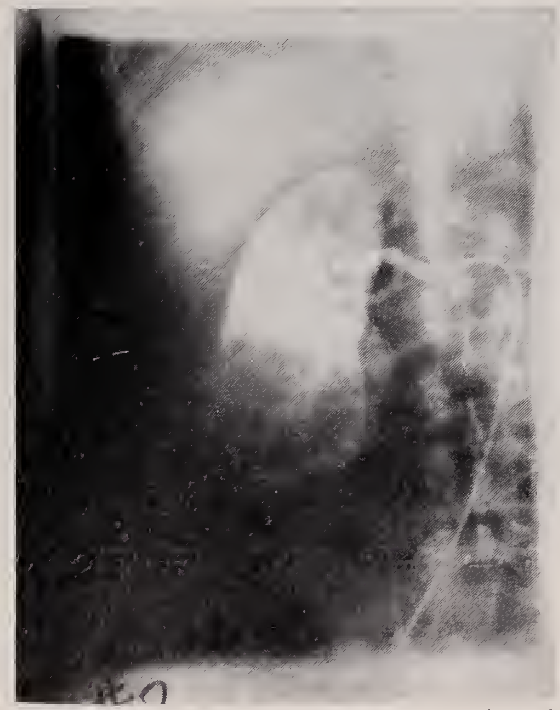

Fig. 1—Lower pole mass, right kidney, at arteriography (Case 2).

---

*Fourth year medical student, University of Minnesota Medical School, Rural Physician Associate Program, Minneapolis.

†Internist, Willmar Medical Center and Associate Professor, Clinical Medicine, Department of Internal Medicine, University of Minnesota Preceptor, Rural Physician Associate Program, Minneapolis.

#Urologist, Willmar Medical Center, Willmar, Minnesota.

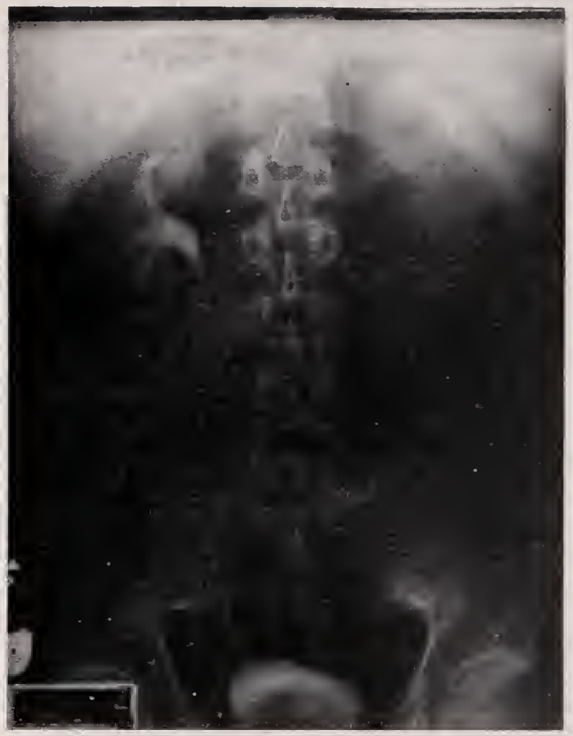

Fig. 2—Inconclusive IVP suggesting an indefinite left renal outline (Case 2).

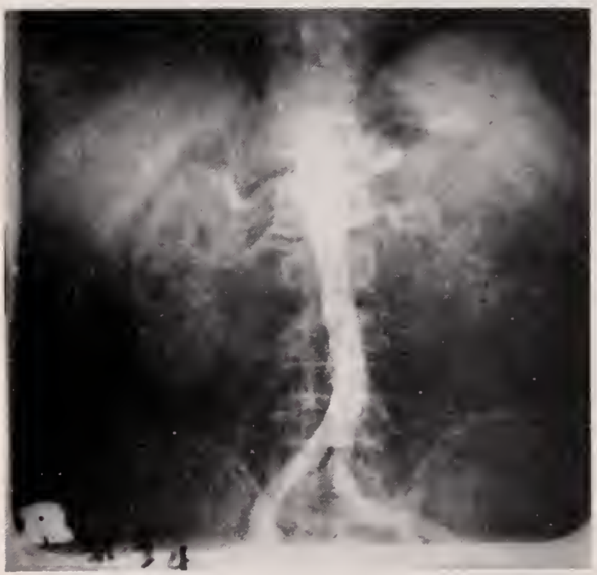

Fig. 3—Left renal tumor at arteriography (Case 4).

Pathologic examination revealed a 601 gm tumor and vascular invasion.

Case 5

A 65-year-old male with amyotrophic lateral sclerosis and coronary artery disease was seen with urinary symptoms including frequency, hesitancy, nocturia, and difficulty in maintaining the urinary stream. His medical record indicated that Valium, 40 mg. per day, had been prescribed. Examination revealed mild enlargement of the prostate gland. Hb was 13.7 gm%. Urinalysis showed occasional red blood cells. IVP revealed a right renal mass, confirmed by arteriography. A 10 x 5 x 5 cm. multilobular right renal mass which did not penetrate capsule or involve renal vein was found at surgery. It is suggested that the symptoms of prostatism may have been accentuated by Valium prescribed prior to diagnosis, as these symptoms subsequently disappeared after the Valium was discontinued.

Discussion

The "classic triad" of symptoms of hypernephroma, i.e. hematuria, flank mass, and pain, are usually those of advanced disease. Patients with renal cell carcinoma currently are more likely to present with only one or two components of the triad. Occasionally a hypernephroma may even be detected in an asymptomatic individual.

A series of 400 patients with hypernephromas[1] seen at the Mayo Clinic included only 5% with the classical triad; 32% had hematuria, 24% had flank pain, and 34% were found to have a palpable mass. In a series from Aberdeen, Scotland,[2] the "triad" was found in 159 (66.3%) of 240 patients. Hematuria was reported in 18% of the patients of Berger and Sinkoff[3] and in 60% of those in the series of Kaufman and Mims.[4] Flank pain was present in only 14% of the cases of Bottiger and associates[5] while Cox et al.[6] reported 55%. Cox et al. noted that 15% of their patients had a palpable mass; a mass was palpable in 63% of Berger and Sinkoff's cases. The presence of the several symptoms would appear to be related to the pathology. The frequency of reported hematuria likely is related to whether hematuria was gross or only microscopic.

The Mayo series reported a substantial percentage of patients without urinary symptoms (59%) but with findings suggestive of systemic disease: 64% with anemia, 22% with weight loss, 15% with bone pain, 15% with abnormal hepatic function tests, 13% with fever, 6% with cough secondary to lung metastases, and 5% with elevated hemoglobin levels.

The findings in the present series of five cases provides additional evidence which suggests that for many patients with hypernephroma the diagnosis continues to be made only after systemic symptoms are present.

In two instances invasion of the renal vein was present, and in one perirenal fat was involved. The 75-year-old woman in the series with symptoms of weakness and fatigue had a marked iron deficiency anemia, presumably secondary to calyx invasion and unobserved but significant blood loss. The single patient with near-normal hemoglobin level (13.7 gm.%) had no evidence of tumor spread at the time of surgery and the diagnosis was made in the course of diagnostic work-up for presumed prostatism.

Conclusion

The five cases herein reported offer evidence of a changing pattern in symptoms associated with renal cell carcinoma. The classic triad of symptoms likely is associated with advanced local disease. Patients now are more frequently seen with only part of the triad or with systemic symptoms. The intravenous pyelogram may often be considered in evaluation of the patient with less well defined symptoms.

In patients suspected of having a hypernephroma, intravenous pyelogram interpretation as showing a benign cyst should be viewed with caution. Arteriography is recommended in such instances as the occurrence of falsely positive diagnoses is reportedly minimal and false negatives likely also are infrequent.

In the present series of patients, none had the classic triad of symptoms although at least four of the five were anemic at the time diagnosis was made. Efforts to discover the disease earlier and prior to the appearance of gross hematuria, anemia, or an obvious flank mass may improve the outcome for those with this disease.

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*Our Retiring Family Doctor**

Who's going to come running at the drop of a hat;
when we call him to say we have this or that?

Who will look thru his bifocals, right down his nose;
and quietly says, "just take off your clothes?"

Who's going to look in our throats, eyes and ears;
to find out the causes for all of our fears?

Who's going to listen to all our heart beats;
and says, "stop smoking and cut out the sweets?

Who's going to give us the needle and calmly say;
"lots of liquids, these pills and see me on Tuesday?"
Nobody
His appointment book is closed, much to our chagrin;
no one to ask us, "well, how have you been?"

So now he can relax, travel, golf and read;
He certainly has it coming—so God speed.

Alta Mae Dowdell

---

*On occasion of retirement of A. Harold Mork, M.D., Coon Rapids, Minnesota.

Parathyroid Adenoma Presenting as a "Cold Nodule" on Thyroid Scan

ROBERT S. LUND, M.D.* and REX B. SHAFER, M.D.*

A 55-year-old patient is described, who presented with a 2 x 2 cm neck mass and was found to be clinically hyperparathyroid. A ^{131}Iodine scan of the thyroid revealed a large "cold nodule." At surgery, a five gm mass was removed which was thought to be typical thyroid adenoma, but proved to be parathyroid adenoma on microscopic examination. The literature on parathyroid adenomas is reviewed and emphasis is placed on the differential diagnosis of a large "cold thyroid nodule."

^{131}Iodine scanning of the thyroid is widely used in the evaluation of neck mass. Demonstration of a "cold" or non-functioning solitary nodule raises suspicion of malignant disease. The incidence of thyroid carcinoma in such cases is reported to be as high as 55%.[1] The differential diagnosis of "cold thyroid nodule" includes non-functioning thyroid adenoma, hemorrhage, necrosis or degeneration within the gland, thyroid or parathyroid cyst and, in one reported case,[2] intrathyroid non-chromaffin paragangliomatosis.

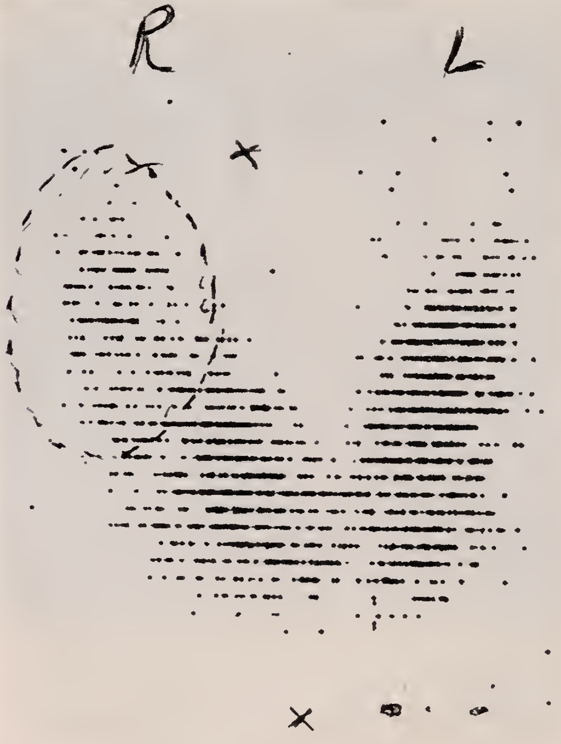

Fig. 1—^{131}I rectilinear scan of thyroid demonstrates "cold nodule" in right lobe of thyroid.

We recently encountered an unusual benign cause of a "cold thyroid nodule" in a patient whose large parathyroid adenoma sufficiently displaced thyroid tissue to present as a "cold" area on ^{131}I scanning. A review of the literature revealed only four other similar cases. Three of these were in patients clinically hyperparathyroid and who were correctly diagnosed prior to surgery as having palpable parathyroid adenomas.[1,3,4] The fourth was diagnosed postoperatively in an asymptomatic patient who was explored for a "thyroid nodule" and histologically found to be parathyroid adenoma.[5]

Case Report

A 55-year-old salesman with a long history of recurrent ulcer disease was referred for evaluation and treatment. On physical examination, a 2 x 2 cm firm right neck mass was found. The thyroid scan showed a large "cold" nodule in the right upper pole (Figure 1). Evaluation of thyroid function included a 24 hour RAI uptake of 10% (nl 9-34%), T_3 resin sponge uptake of 23% (nl 25-35%), and a total T_4 of 10.2 μgm% (nl 6-12.5 μgm%). The initial serum calcium was 13.0 mg%, serum phosphorus 2.3 mg%, serum albumin 4.8 mg% and serum chloride 110 meq/l. Dehydration in preparation for upper gastrointestinal examination was associated with elevation of serum calcium to 15.6 mg% and a decreased serum phosphorus of 1.6 mg%. The patient was considered clinically hyperparathyroid in spite of a normal alkaline phosphatase of 69 I.U. Serum parathyroid hormone was reported at 1.5 ng/ml (nl 0-1.5 ng/ml) and tubular reabsorption of phosphate was measured at 30% (nl 85-100%). These further substantiated the clinical impression of hyperparathyroidism. Radiographic study of the skull, clavicles, hands and kidneys, however, failed to reveal the typical findings of hyperparathyroidism.

---

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See editorial, page 465.

The preoperative diagnosis was hyperparathyroidism and right thyroid nodule. At surgery the right lobe of the thyroid was removed. Attached to the mid-lateral edge of the thyroid was a 2.5 cm round, 5.2 gm mass with a thin fibrous capsule (Figure 2). This was grossly thought to be a thyroid adenoma, but histologically it proved to be a large parathyroid adenoma. The patient's postoperative course was uneventful. His serum calcium showed progressive decrease to 8.6 mg% at the time of discharge on the sixth post-operative day. When the patient was seen again three weeks later, his serum calcium and phosphorus were found to be normal and he was clinically well.

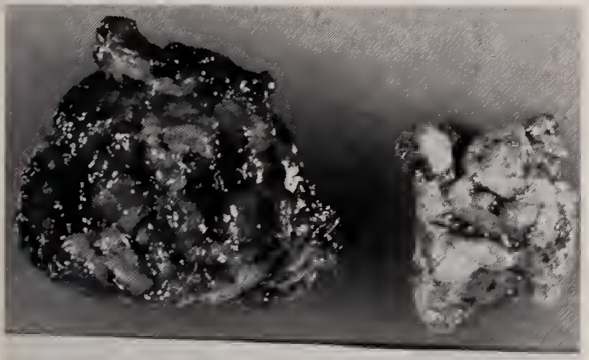

Fig. 2—At surgery, a 5.2 gm rounded mass with thin, fibrous capsule was removed. Pathologic specimen is shown here in two pieces.

Discussion

When a palpable neck mass is studied by ^{131}I scanning of the thyroid gland and a "cold nodule" is found, thyroid carcinoma must be considered. This is true even if the patient has clinically documented hyperparathyroidism. Palpable parathyroid adenomas, however, though unusual, are not rare. It is reported that 5% of parathyroid adenomas are palpable.[6] This suggests that serious consideration should be given this diagnosis in a patient with a neck mass and coincident hyperparathyroidism.

Parathyroid adenomas vary greatly in size from 100 mg to 50 gm, with one extreme case of a 300 gm tumor on record.[7] Adenomas of three or more grams may, depending on their relationship to the thyroid, produce a "cold" area on the scan. The previously reported examples of this phenomenon were due to tumors weighing 3.5 gm,[3] 22 gm,[4] and 34 gm.[1]

Charity Hospital of Louisiana reported its experience[8] with 96 parathyroid adenomas and found an age range from 15 to 92 years, with the peak incidence in the sixth decade. They found no difference in incidence between the black and white population, but reported a somewhat higher frequency in women. The anatomic locations of 84 adenomas in 76 patients were available by chart review. Sixty-one percent of these were behind the lower poles of the thyroid, while only 21% were located behind the upper poles. Five percent were retrosternal, 4% were within the thyroid and the remainder were scattered in intermediate positions behind the thyroid.

A multiplicity of techniques have been developed for preoperative localization of parathyroid adenomas. These include selective angiography, thermography and scanning with ^{75}Se-labelled methionine or ^{75}Se-toluidine blue. Varied experience is reported with these techniques and little is as yet available by way of comparative value. To date, no instances of palpable parathyroid adenomas using these techniques have been reported.

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Uterine Prolapse and Upper Urinary Tract Obstruction

T. A. HILDRETH, M.D.;* WILLIAM STEWART, M.D.* and A. S. CASS, M.D.*

Prolapse of the uterus causing upper urinary tract obstruction is a well-documented, but poorly appreciated clinical entity. Two cases are presented and the literature reviewed. Urologic evaluation is indicated in females with uterine prolapse.

PROLAPSE OF THE UTERUS causing upper urinary tract obstruction is a well-documented clinical entity.[1-9] This report demonstrates the marked degree of obstruction that can occur and the rapid improvement which follows adequate treatment of the uterine prolapse.

Case Reports

Case 1

A 69-year-old white female para 3003 underwent a vaginal hysterectomy, A-P repair, and urethral plication in May, 1972 for symptoms of stress incontinence. A preoperative IVP was normal (Figure 1). One month after surgery she was noted to be a surgical failure with marked vaginal problems.

The patient was lost to follow-up until June, 1974 when she was hospitalized for evaluation of right upper quadrant pain. The marked vaginal prolapse was still present and an intravenous pyelogram revealed bilateral upper tract obstruction with pyelocalyectasis and uterectasis especially on the right side (Figure 2). Renal function was normal with a BUN of 10 and serum creatinine of 1.2.

In July, 1974 a vaginal pessary was placed. A follow-up IVP in May, 1975 showed normal urinary tracts (Figure 3).

Case 2

A 73-year-old white female, para 7003 presented in November, 1973 with a four year history of stress incontinence, recurrent urinary tract infections and cystocele. An IVP at that time revealed dilated upper urinary tracts, especially on the right side. An IVP which was performed in January, 1969 revealed normal upper urinary tracts.

Treatment of the uterine prolapse by vaginal pessary was unsuccessful due to vaginal pain and bleeding requiring intermittent removal of the pessary. Her BUN was 28, serum creatinine 2.3, and creatinine clearance 39 L/min.

An IVP in January, 1974 revealed non-visualization on the right and moderate pyelocalyectasis with ureterectasis on the left (Figure 4). The patient then underwent a vaginal hysterectomy and cystocele repair. The stress

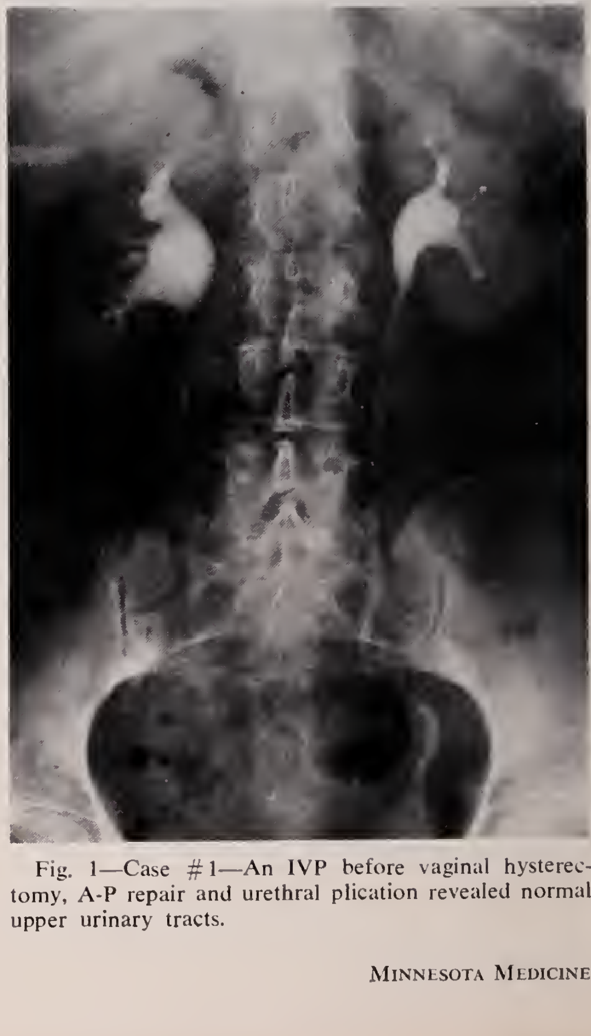

Fig. 1—Case #1—An IVP before vaginal hysterectomy, A-P repair and urethral plication revealed normal upper urinary tracts.

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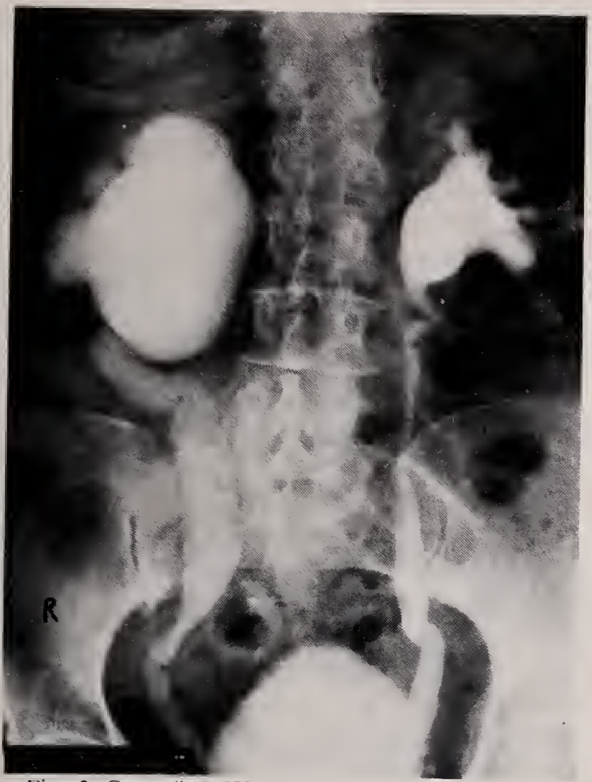

Fig. 2 Case #1—IVP showing bilateral upper urinary tract obstruction especially on the right side.

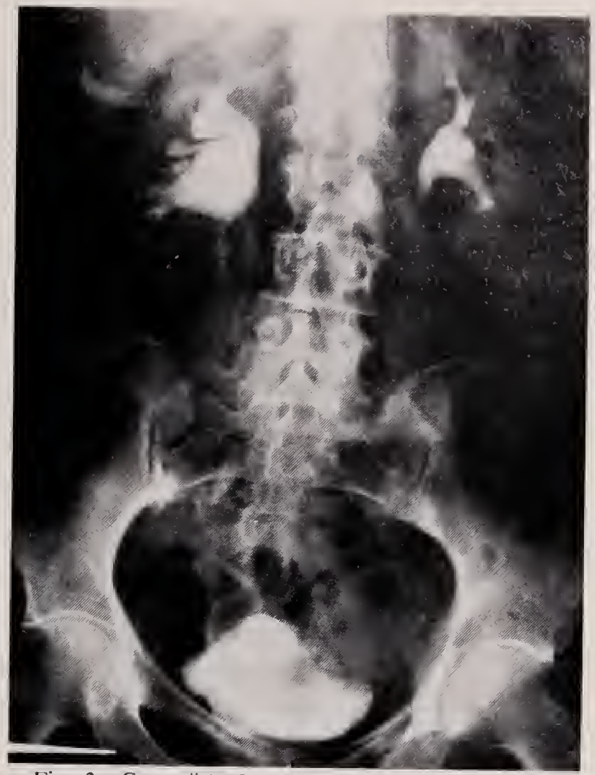

Fig. 3—Case #1—Follow-up IVP ten months after use of vaginal pessary showing normal upper urinary tracts.

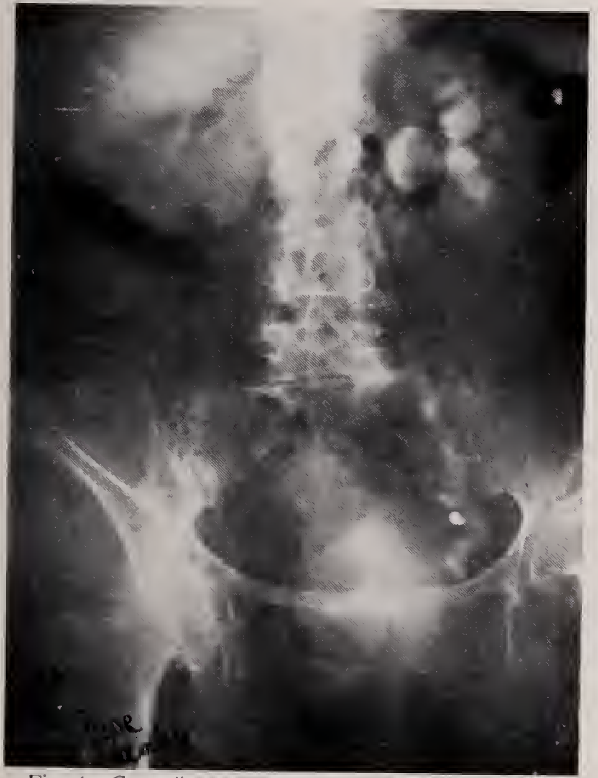

Fig. 4—Case #2—Repeat IVP in January, 1974 after unsuccessful use of vaginal pessary revealed non-functioning right kidney and dilated left upper urinary tract.

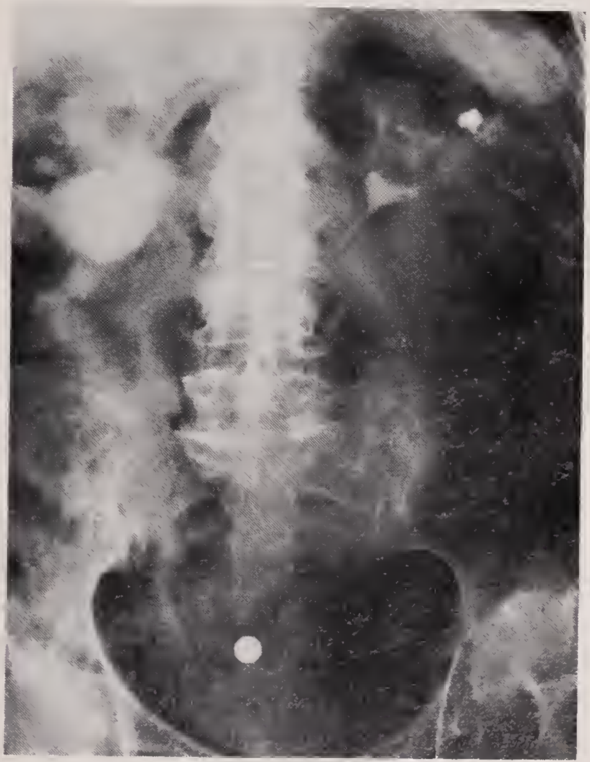

Fig. 5—Case #2—Follow-up IVP after vaginal hysterectomy and cystocele repair showed bilateral function with normal left upper urinary tract and some dilatation on right side.

incontinence disappeared and she has been free of urinary tract infections. A follow-up IVP revealed bilateral function with normal left upper tract and some dilatation on the right side (Figure 5). A BUN was 25.

Discussion

Rudin[1] and associates reviewed patients with uterine prolapse and found an incidence of seven percent with upper urinary tract obstruction on excretory urography attributable to the prolapse.

Elkin[2] et al. reported a 74 percent incidence of urinary tract infection in females with upper urinary tract obstruction due to uterine prolapse. The diagnosis of upper urinary tract obstruction could only be made by excretory urography with prone and erect films as 15 of the 19 patients had normal blood urea nitrogen.

Mueller-Heuback[3] reported three fatal cases of third degree uterine prolapse associated with pronounced hydronephrosis and/or pyelonephritis and uremia. Other authors[4-9] have found a high incidence (30-80%) of advanced renal disease associated with uterine prolapse.

Compression of the ureters outside the bladder is thought to be the cause of the ureteral obstruction. With uterine prolapse the uterine vessels are stretched, acting as slings over and about the ureters, thereby obstructing them. Another explanation has been caudal displacement of the trigone resulting in mechanical deformity and narrowing of the ureteral orifices.[2]

This upper urinary tract obstruction as a result of uterine prolapse is a well-documented, but poorly appreciated and infrequently anticipated complication of the uterine prolapse.

Our two patients illustrate the reversibility of the upper urinary tract obstruction when the uterine prolapse is adequately corrected either by surgical repair or pessary placement. A urologic evaluation, especially including a intravenous pyelogram, is mandatory with uterine prolapse.

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Medical Alumni of Hennepin County Medical Center

A reunion of all medical alumni of Hennepin County Medical Center (Minneapolis General Hospital, Hennepin County General Hospital) will be held in Minneapolis October 14, 15 and 16, 1976. For information, write to Eldon Berglund, M.D., Hennepin County Medical Center, Minneapolis, Minnesota 55415.

Northwestern Pediatric Society
Annual Meeting—September 17, 1976

The annual meeting of the Northwestern Pediatric Society wil be held Friday, September 17, 1976 at the Chanhassen Dinner Theater, Chanhassen, Minnesota.

Original papers will be presented and the guest speaker for the occasion will be Charles L. Scriver, M.D., geneticist with the McGill University and Montreal Children's Hospital. Dr. Scriver's subject will be "Genetics: A Voyage to Discovery."

Contact: Ray C. Hippchen, M.D., Secretary-Treasurer, 730 E. County Road B., St. Paul, Minnesota 55117.

Cerebellar Hemorrhage

FREDERICK M. VINCENT, M.D.*

Ten percent of all intraparenchymal intracranial hemorrhages are cerebellar in location. Thus, they are not as uncommon as previously thought. In the past most cerebellar hemorrhages have been diagnosed at postmortem examination. Unfamiliarity with this condition has led to its frequent misdiagnosis. Clinical, diagnostic, therapeutic and pathological aspects of cerebellar hemorrhage are discussed and features that should help in its rapid diagnosis are described.

CASE REPORTS OF cerebellar hemorrhage date back to 1813.[1] The first American case was not reported until 1858.[2] During the ensuing 74 years reports of this entity appeared in the literature sporadically. In 1932, Michael[3] reported on 17,257 autopsies performed at the University of Minnesota from 1897 to 1931. There were 1112 parenchymal intracranial hemorrhages in this series and 10 of these (0.9%) were cerebellar. Since then other large post-mortem series have been reported with incidence ranging from 9.0 to 13 percent (Table 1).[4-7] It was evident from these and other series that the diagnosis of cerebellar hemorrhage was first made only postmortem.

Recent statistics indicate that cerebellar hemorrhage is far from rare, the overall incidence being 10 percent of all intracranial, intraparenchymal hemorrhages.[4,8,9] This percent is expected on the basis of the weight ratio of the cerebellum to the remainder of the brain[4,9] as the cerebellum represents 10 percent of the brain's total weight. The fact that hemorrhage into the brain stem exceeds cerebellar hemorrhage by a two to one margin appears to refute the view[10] that the weight ratio alone accounts for the frequency of cerebellar hemorrhage, but necropsy data are in accord with this view.

Cerebellar hemorrhage carries a grave prognosis, about 75 percent of medically treated cases expire within the first few days, whereas those treated surgically have a much better survival.[11,12] Selection may, however, account for these differences in prognosis. Reliable rules have to be established for the identification of acute cerebellar hemorrhage, if surgical decompression can actually alter the poor prognosis.[3,6,7,11-13] The purpose of this paper is to identify the symptoms and signs that may indicate the presence of a cerebellar hemorrhage, so that confirming diagnostic tests and therapy may be undertaken.

Clinical Features and Causes

Cerebellar hemorrhage can occur at any age but the higher incidence is in the 6th and 8th decades of life.[7,8,11,12] These ages coincide with the highest incidence of intracerebral hemorrhage of all types.[14] There seems to be a male preponderance, perhaps reflecting the higher incidence of hypertension in the male.[13] Arterial hypertension is the commonest predisposing factor in cerebellar hemorrhage, being present in 50-70

TABLE 1
Frequency of Cerebellar Hemorrhage in Autopsy Series

Author (year)	Number of Autopsies	Total no. of Intracranial Hemorrhages	No. of Cerebellar Hemorrhages	% of Cerebellar Hemorrhages
Mitchell & Angrist[4] (1942)	38,881	115	15	13.0
Grendahl[5] (1958)	7,684	455	51	11.2
Rey-Bellet[6] (1960)	4,526	224	20	9.0
Dinsdale[7] (1964)	19,093	511	52	10.2

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See editorial, page 464.

percent of the cases reported.[4,10,12] Angiomatous malformations account for the majority of cerebellar hemorrhages in the younger age groups.[15] Other etiologic factors recorded more recently are listed in Table 2.[11] Older reports indicated that cerebellar hemorrhage commonly was due to arteriosclerosis or syphilis, with diabetes, acute infectious processes, alcoholism, epilepsy, trauma, and aneurysms being less frequently implicated.[3,4,16]

TABLE 2
Etiologic Factors in Cerebellar Hemorrhage

Etiology	Number of Cases (%)
Hypertension	35 (62)
Anticoagulation	8 (14)
AV Malformation	2 (4)
Blood Dyscrasie	2 (4)
Tumor	1 (2)
Trauma	1 (2)
Unknown	7 (12)

The most common symptoms on admission to the hospital are listed in Table 3.[11,12] Repeated bouts of vomiting are characteristic.[12,17] Headache is also common. It may be abrupt in onset and excruciating.[11] It is frequently bioccipital in location,[11,12] perhaps due to traction on pain sensitive structures in the posterior fossa. Headache can also be generalized or frontal in location,[14,17] perhaps due to the development of acute internal hydrocephalus.[10,14] Dizziness and the inability to stand or walk ("cerebellar astasia-abasia"[12]) are also prominent symptoms.[11,12] Loss of consciousness is unusual at the onset, but, as the hemorrhage progresses, coma is common.[11,12,14] Other less frequently reported symptoms are dysarthria, ataxia, and dysphasia.[11,12] Typically the clinical picture develops over a period of several hours. The major signs frequently observed on admission in non-comatose patients are listed in Table 3.[11,12,14] The arterial blood pressure is commonly elevated in those patients with hypertensive hemorrhage. Hematologic abnormalities are found in patients with a blood dyscrasia, commonly prolonged prothrombin time or thrombocytopenia.

TABLE 3
Clinical Picture on Admission

Symptoms	Signs
Nausea and vomiting	Gait ataxia
Headache	Trunkal ataxia
Dizziness	Appendicular ataxia
Inability to stand or walk	Babinski sign
Dysarthria	Peripheral 7th nerve palsy
Ataxia	Dysarthria
Dysphasia	Gaze palsy
	Nystagmus
	Nuchal rigidity

Respiratory abnormalities have been reported to be a grave omen.[14] Respiration may be normal in the early phase, but with the progression of the hemorrhage, Cheyne-Stokes respirations develop.[14,18] In terminal stages, respirations become deeper, faster, and ataxic.[12]

Abnormalities of the ocular system are helpful in diagnosis.[12,14] Pupils may be of normal size, but most commonly, they are miotic (2 mm) and remain small into the early stages of coma.[12,14] They are usually equal, but on careful examination the pupil on the side of the lesion may be slightly smaller.[12] They usually react to bright light until a late stage of stupor.[12] Paresis or paralysis of conjugate lateral gaze to the side of the lesion is a common finding. A sixth nerve paresis sometimes precedes gaze palsy.[12] Horizontal nystagmus to the side of the lesion may be present in up to fifty percent of cases.[12,14] Internuclear ophthalmoplegia with associated ptosis of one eye has been reported in cases of cerebellar hemorrhages, and described as "involuntary closure of one eye."[12] Skew deviation may be present.[12] In cases without associated internuclear ophthalmoplegia, the lesion is frequently ipsilateral to the lower eye.[19]

The absence of a Babinski sign bodes well for the survival of the patient. However, Babinski signs are frequently present.[12,14]

Hemiplegia may be present, but it is of questionable significance.[6,12,14] It may indicate a previous stroke.[12] The decreased spontaneous movements of ataxic limbs may be confused with weakness.

Comatose patients present a different problem due to their advanced state of brain dysfunction.[11,12] The most common signs are external ophthalmoplegia, respiratory irregularity, and apnea.[11] A minority of comatose patients have lateralizing cranial nerve signs, most commonly ipsilateral seventh nerve palsy.[11]

In the past the triad of constricted and reactive pupils, periodic respirations, and gaze palsy has been regarded as a common feature of cerebellar hemorrhage.[9,14] Recent data[11] suggests that appendicular ataxia, ipsilateral gaze palsy, and peripheral facial nerve palsy may be more diagnostic. At least two of these signs were present in 75 percent of the patients tested in one series.[11] The

TABLE 4
Most Frequently Observed Signs in Cerebellar Hemorrhage

- Appendicular ataxia
- Ipsilateral gaze palsy
- Peripheral 7th nerve palsy
- Constricted and reactive pupils
- Periodic respirations

most common and reliable signs in order of frequency, are listed in Table 4.[11]

Investigations

Lumbar puncture is a guide to the type of lesion but it is dangerous because of the increased intracranial pressure in the posterior fossa and probably should not be performed.[13] However, when performed the fluid is bloody in the majority of cases,[3,6-8,10,11,13,15] and the pressure is usually greater than 180 mm water.[11] A lumbar puncture done too soon after the hemorrhage may not allow enough time for the extravasated blood to reach the subarachnoid space.[9,12] The cerebrospinal fluid may be clear and pressure normal even days after hemorrhage.[9,14]

Electroencephalography and brain scanning are not helpful in aiding rapid diagnosis but carotid arteriography is of great value.[8,11,15] Approximately 85 percent of vertebral arteriograms will disclose signs of a cerebellar mass lesion.[11] The superior cerebellar arteries[8] and inferior vermian vein[20] should be checked specifically for any abnormality in their course.[8] Dinsdale[7] found acute hydrocephalus, occasionally as early as three hours after onset in 75 percent of 52 autopsied cases of cerebellar hemorrhage. Pneumoencephalography will frequently show the absence of air in the fourth ventricle, or signs of a cerebellar mass lesion,[8,14] but this study can precipitate herniation of cerebral substance.[8,14] Computerized transaxial tomography may prove to be the most rapid and reliable method for diagnosing cerebellar hemorrhage and is preferable to the above procedures.[11]

It would be desirable to have x-ray proof of a cerebellar mass but, in many cases, there will not be time to undertake the procedures.[12] Clinical evidence alone may, however, justify exploration of the posterior fossa without additional investigation.[12]

Differential Diagnosis

Approximately two-thirds of the patients with cerebellar hemorrhage may have altered levels of consciousness, but still be responsive when first seen.[11] The diagnosis is more difficult when the cerebellar hematoma is confined to the midline. The latter had a more fulminant course, and ini-

TABLE 5
Differential Diagnosis of Intracranial Hemorrhage*

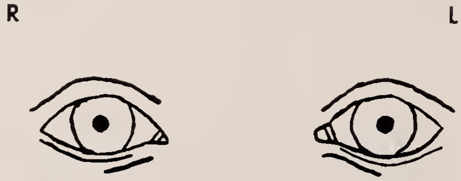
Sign	Cerebellar	Pontine	Thalamic/ Subthalamic	Putamen	Ruptured Aneurysm
Hemiplegia	No	Quadriplegia or bilateral motor signs	Yes	Yes	No
Pupil size	small	small	small	may be normal	variable
Pupillary reaction	Yes	Yes or No	No	Yes	Yes
7th N. palsy		Yes or No			No
-location	ipsilateral		contralateral	contralateral	
-type	peripheral	peripheral	central	central	
Sensory defect	No	Yes	Yes	Yes	No
Conjugate gaze					
palsy	Common	Yes	Uncommon	Yes	No
-side	ipsilateral	ipsilateral	contralateral	contralateral	No
-reversal with ice water	No	No	usually	Yes	No
6th N. palsy	Yes	Yes	Yes	No	No
Hemianopia	No	Yes	Yes, clears early	No	Yes
Vomiting	severe/ repeated	Yes	occasional	occasional	Yes
Unconscious at onset	No	Yes	No	No	Frequently
Subhyaloid hemorrhages	No	No	No	occasional	Yes

*Modified from Fisher.[12]

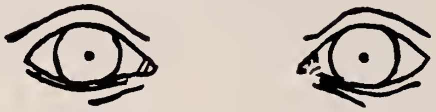
tially had ophthalmoplegia, flaccid quadriplegia, and areflexia.[11]

There are four sites of predilection for hypertensive intracranial bleeding:[12] putamen (60%), thalamus (10%), pons (10%), and cerebellum (10%). In the presence of bloody spinal fluid, cerebellar hemorrhage has to be differentiated from intraparenchymal hemorrhage of the putamen ,thalamus, and pons (Table 5).[12] Eye signs are of diagnostic help (Figure 1).[12,21]

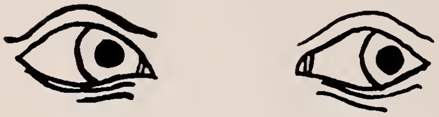
The presence of hemiplegia, hemisensory defect, facial weakness, hemianopsia, and conjugate deviation of the eyes to the side of the lesion (reversible by ice-water irrigation of the opposite ear) point to the putamen as the site of the hemorrhage.[12]



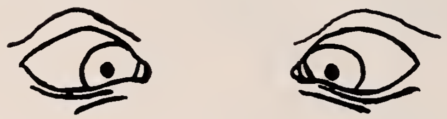
a. - Cerebellar Hemorrhage



b. - Pontine Hemorrhage



c. - Left Putaminal Hemorrhage



d. - Thalamic Hemorrhage

Fig. 1—Ocular Signs of Intracranial Hemorrhage: (a) *Cerebellar Hemorrhage*—ipsilateral conjugate gaze palsy. A 6th nerve palsy or skew deviation may be present. Pupils may be normal size and reactive, but often are miotic (2 mm). (b) *Pontine Hemorrhage*—eyes are midposition and oculocephalic reflexes are absent. Ocular bobbing may be present. Pupils are pinpoint, but react to bright light. (c) *Left Putaminal Hemorrhage*—eyes deviate to the side of the lesion. Pupils are of normal size and reactive. (c) *Thalamic Hemorrhage*—downward deviation of the eyes (look at the nose). Vertical gaze may or may not be impaired. Pupils are small and nonreactive.

Thalamic hemorrhage may produce both hemiplegia and hemisensory loss with downward deviation of the eyes at time associated with paralysis of vertical gaze.[12] The pupils are commonly small and usually do not react to bright light. Anisocoria may be present.

In pontine hemorrhage the patient usually becomes rapidly comatose and develops flaccid quadriplegia and hyperthermia.[12] Pupils are pinpoint but reactive, and ocular bobbing[22] may be present. Conjugate gaze palsy which does not respond to ice-water irrigation may also appear.[7,12,14]

Syncope, third nerve palsy, subhyaloid hemorrhage, and hemiplegia are common findings associated with rupture of an intercranial aneurysm.[13]

Clinical Course

According to Michael,[3] the clinical course of cerebellar hemorrhage may be "fulminating," "grave," or "benign." In the first type there is abrupt onset of coma and frequently sudden death. There is a rapidly progressive downhill clinical course and cerebellar signs may be absent.[3,8,12,14] Respirations are irregular, pupils pinpoint, and oculovestibular reflexes are absent. This class represents 10 to 20 percent of all cerebellar hemorrhage.[14] "There are no premonitory signs, or at most the patient may utter a brief cry and place the hand at the nape of the neck. He falls over and death is practically instantaneous. Some patients are found dead."[3]

Cases of the second type have a gradual deterioration. Frequently, premonitory signs are present. Early in the progression of the hemorrhage nystagmus and ocular signs may appear and assist in the diagnosis[3,4] but abrupt cessation of respiration may occur.[12] Alertness may rapidly change to drowsiness, stupor, and coma.[12] Death usually occurs within 48 hours,[3,14] and up to 60 percent of patients died within two days in one series.[7] Patients in the second category benefit most from early diagnosis and the appropriate neurosurgical intervention.[12,14]

Patients with the benign type can have a prolonged survival, but late deterioration may occur. Severe impairment of consciousness sometimes develops after several days delay. Death may result from acute hydrocephalus, increased intracranial pressure, or tonsillar herniation.[14] Most cases treated surgically have been from this category.

Stupor and coma tend to be irreversible; 19 of 20 patients in one series died.[11]

Treatment

Immediate surgery is imperative if the diagnosis is made, especially in those patients with grossly altered levels of consciousness.[8,12,17] Patients with coexistant hypertension or coagulation abnormalities should be treated to reduce blood pressure and correct the coagulopathy. The single most important factor influencing the surgical outcome is the level of consciousness before the operation.[14] In Ott's[11] series, 17 percent of those alert or drowsy before the operation expired, compared to 75 percent of those who were stuporous or comatose. In general, patients either improved rapidly in mental status and survived operation or died within a few hours of operation.

Suboccipital craniotomy is the surgical approach of choice.[12,14] When the dura is opened, the large swollen hemisphere may bulge out. Simple incision will result in evacuation of the clot.[12] It is important to monitor blood pressure as the patient awakens from anesthesia and in the immediate post-operative recovery period.

Anatomy and Pathology

Cerebellar hemorrhage is more apt to be fatal than cerebral hemorrhage because of the proximity of the former to medullary centers[7] and the confining effects of the tentorium. If a hematoma is formed, obstruction to cerebrospinal fluid pathways leads to hydrocephalus and increased intracranial pressure.[24]

The cerebellum develops from vestibular structures by the addition of a series of lobes which acquire an extensive blood supply.[23] The anterior and superior surfaces of the cerebellum and its deep nuclei are supplied by the superior and inferior cerebellar arteries which are branches of the basilar artery. The posterior and inferior surfaces are supplied by the posterior inferior cerebellar artery which is a branch of the vertebral artery.[3,23]

Most hypertensive cerebellar hemorrhages arise in or near the dentate nucleus (Figure 2). Although some report a left-sided predominance[7,12] others indicate that hemorrhage occurs in each cerebellar hemisphere with equal frequency.[3,7] The "artery of hemorrhage" for the cerebellum is the branch to the dentate nucleus from the superior cerebellar artery.[3,4,24] Due to the lamellar structure of the cerebellum, blood often dissects into the cerebellar cortex and adjacent structures[23] producing considerable compression and destruction of gray and white matter. The hemorrhage may extend into the cerebellar peduncle and may sometimes rupture into the brain stem.[24] The hematoma varies in size frequently being over five cm in its largest diameter,[12,24] and is usually large enough to cause death from medullary compression. Blood can extend into the subarachnoid space or the fourth ventricle[7] and tends to escape into the cisterna magna. A large hematoma may occlude the aqueduct of Sylvius and cause internal hydrocephalus. These features contribute to the elevated intracranial pressure which causes cerebellar coning.[24] Upward transtentorial displacement of the cerebellum with large hematomas can occur, and uncal herniation is attributed to internal hydrocephalus.[24]

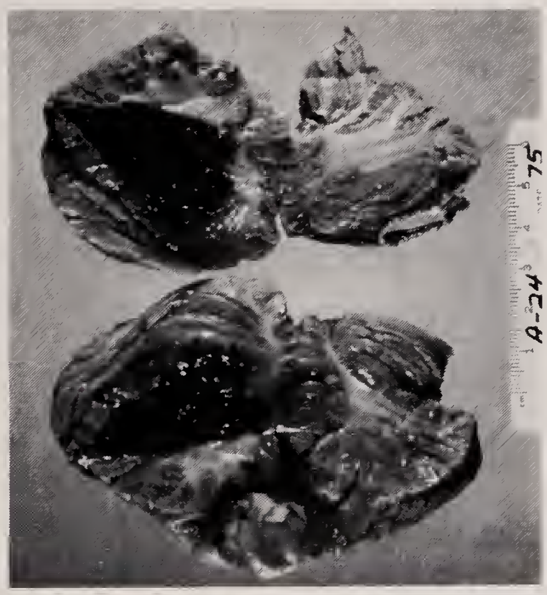


Fig. 2—Typical hypertensive cerebellar hemorrhage in the vicinity of the left dentate nucleus.

Cerebellar hemorrhage from various causes may start anywhere in the cerebellar hemispheres or near the vermis. Cerebellar angiomatous malformations are usually deep in the hemisphere. Their size varies, but they are usually larger than two cm and consist mainly of thin walled veins, usually without arteriovenous communication.[24]

Occasionally there is no gross evidence of the cause of the hemorrhage.[10,25] Such cases are called "spontaneous" intracerebellar hemorrhages. They are uncommon.[24,25] In some cases, a cryptic vascular formation is the cause of the cerebellar hemorrhage,[25] the feeding artery of which may be a major sized vessel. Cryptic malformations resemble angiomatous malformations in their neuropathology. However, even when no malformation is discovered, the abnormal vessels may have been destroyed by the hematoma.[25]

Summary

The etiological, clinical, and pathological features of cerebellar hemorrhage have been discussed. Cerebellar hemorrhage accounts for 10 percent of all intracranial, intraparenchymal bleedings and is not as rare as is commonly thought. Most cases are secondary to hypertension and occur in the 6th to 8th decades of life. Those that occur in younger patients are often secondary to angiomatous malformations or blood dyscrasias.

Headache, repeated bouts of nausea and vomiting, and the inability to stand or walk are the most common symptoms noted on admission to the hospital. The most frequently observed signs are ipsilateral gaze palsy, peripheral facial nerve palsy, and appendicular ataxia.

Computerized axial tomography or vertebral angiography are the best diagnostic procedures. Suboccipital craniotomy with evacuation of the hematoma is the preferred surgical procedure. The most important factor affecting surgical outcome is the level of consciousness before the operation. With coma the operative mortality approaches 75 percent. Early diagnosis and surgical treatment can reduce mortality.

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American Diabetes Association of Minnesota

The American Diabetes Association of Minnesota announces that applications are now being accepted for grants in diabetes research to be awarded in the fall of 1976. Grants available are: Small Grants of up to $5,000 for one year; Large Grants up to $20,000 per year for one to three years.

For further information contact:

The American Diabetes Association of Mn.
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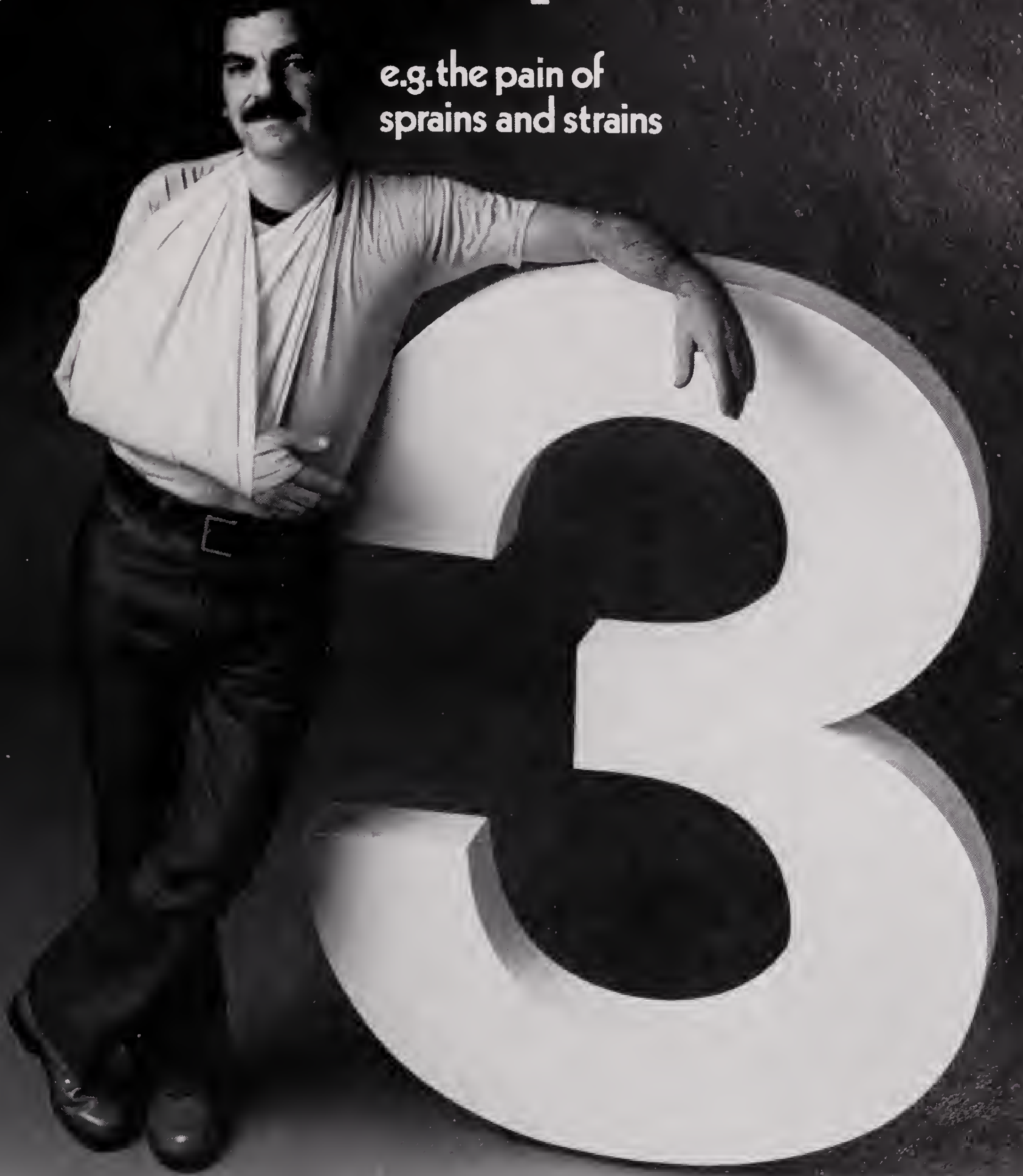

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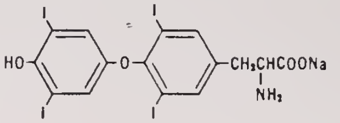

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Actions: SYNTHROID (sodium levothyroxine) **Tablets,** taken orally, provide hormone that is readily absorbed from the gastrointestinal tract SYNTHROID **Injection** is effective by any parenteral route. Following absorption, the synthetic L-thyroxine provided by SYNTHROID products cannot be distinguished from L-thyroxine that is endogenously secreted. Each is bound to the same serum proteins and each exhibits a six to seven day circulating half-life in the euthyroid individual

Both SYNTHROID products will provide L-thyroxine as a substrate for physiologic deiodination to L-triiodothyronine. Therefore, patients taking SYNTHROID products will demonstrate normal blood levels of L-triiodothyronine even when the thyroid gland has been surgically removed or destroyed by radioiodine. Administration of levothyroxine alone will result in complete physiologic thyroid replacement.

Indications: SYNTHROID (sodium levothyroxine) products serve as specific replacement therapy for reduced or absent thyroid function of any etiology. SYNTHROID **Injection** can be used intravenously whenever a rapid onset of effect is critical, and either intravenously or intramuscularly in hypothyroid patients whenever the oral route is precluded for long periods of time.

Contraindications: There are no absolute contraindications to SYNTHROID (sodium levothyroxine) therapy. Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis. (See WARNINGS)

Warnings: Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met. Clinical judgment will then dictate either a less-than-complete restoration of thyroid status or reduction in thyroid dosage.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. SYNTHROID (sodium levothyroxine) therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders.

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

Precautions: Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule. With SYNTHROID (sodium levothyroxine) **Tablets,** the relatively slow onset of action minimizes the risk of overdose but close observation in the weeks following institution of a dosage regimen is advised. Treatment of thyroid hyperactivity induced by oral medication is confined to interruption of therapy for a week, followed by reinstitution of daily therapy at an appropriately reduced dosage.

Adverse reactions: Adverse reactions are due to overdose and are those of induced hyperthyroidism.

Dosage and administration: For most adults, a final dosage of 100 mcg (0.1 mg) to 200 mcg (0 2 mg) of SYNTHROID (sodium levothyroxine) **Tablets** daily will restore normal thyroid function and only occasionally will patients require larger doses Failure to respond adequately to a daily oral intake of 400 mcg (0.4 mg) or more is rare and should prompt reconsideration of the diagnosis of hypothyroidism, special investigation of the patient in terms of malabsorption of L-thyroxine from the gastrointestinal tract or poor adherence to therapy.

The concomitant appearance of other diseases, especially cardiovascular diseases, usually dictates a replacement regimen with initial doses smaller than 100 mcg/day (0.1 mg).

In otherwise healthy adults with relatively recent or of hypothyroidism, full replacement dose of 150 mc (0.15 mg) or 200 mcg (0.2 mg) has been instituted immediately without untoward effect and with good therapeutic response. General experience, however, favors a more cautious approach in view the possible presence of subclinical disorders of the cardiovascular system or endocrinopathies.

The age and general physical condition of the patie as well as the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. In the elderly patient with long standing disease, evidence of myxedemat infiltration and symptomatic, functional or electrocardiographic evidence of cardiovascular dysfunction, the starting dose may be as little as 25 m (0.025 mg) per day Further incremental increases of 25 mcg (0.025 mg) per day may be instituted at th to four week intervals depending on patient response. Conversely, otherwise healthy adults may be started at higher daily dosage and raised to the full replacement dosage in two to three weeks. Clearly it is the physician's judgment of the severity of the disease and close observation of patient response which determines the rate of dosage titration.

Laboratory tests to monitor thyroid replacement therapy are of limited value. Although measurement of normal blood levels of thyroxine in patients on replacement regimens frequently coincides with t clinical impression of normal thyroid status, higher than normal levels on oral replacement of levothyroxine occasionally occur and should not be considered evidence of overdosage per se.

In all cases, clinical impression of the well-being of th patient takes precedence over laboratory determination in determining the appropriate individual dosage.

In infants and children, there is a great urgency to achieve full thyroid replacement because of the critic importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body siz the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult, as much as 300 mcg (0.3 mg) to 400 mcg (0.4 mg) per day.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of SYNTHROI **Injection** may be administered intravenously as a solution containing 100 mcg/ml. Although the patient may show evidence of increased responsivity within six to eight hours, full therapeutic effect may not be evident until the following day. An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvement has not occurred Like the oral dosage form, SYNTHROID **Injection** produces a predictable increase in the circulating level of hormone with a long half-time. This usually precludes the need for multiple injections but continued daily administration of lesser amounts intravenously should be maintained until the patient fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine intravenously is clearly not without its cardiovascular risks. Under such circumstances, intravenous therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgment in this situation may dictate smaller intravenous doses of levothyroxine.

SYNTHROID **Injection** by intravenous or intramuscul routes can be substituted for the oral dosage form when ingestion of SYNTHROID **Tablets** is precluded for long periods of time.

How Supplied: SYNTHROID (sodium levothyroxine) **Tablets** are supplied as scored, color-coded compresse tablets in 6 concentrations: 25 mcg (0.025 mg)—orang . . . 50 mcg (0.05 mg)—white . . . 100 mcg (0.1 mg)—yellow . . . 150 mcg (0.15 mg)—blue . . . 200 mcg (0.2 mg)—pink . . . 300 mcg (0.3 mg)—green.

SYNTHROID (sodium levothyroxine) for **Injection** is supplied in 10 ml vials containing 500 mcg of lyophilized active ingredient and 10 mg of Mannitol. U.S.P. A separate 5 ml vial containing Sodium Chloride Injection, U.S.P is provided as a diluent.

Directions for reconstitution: Reconstitute the lyophilized sodium levothyroxine by aseptically addin 5 ml of the Sodium Chloride Injection, U.S.P to the vial. Shake vial to insure complete mixing **Use immediately** after reconstitution. Discard any unused portion.

U.S. Pat. 2,889,363

January 1975

Editorials

The Proud Profession

proud/praud/adj [ME, fr. OE prud. prob. fr. OF prod, prud, prou capable, good, valiant, fr. LL prode advantage, advantageous, back-formation fr. L prodesse to be advantageous, fr. pro-, prod- for, in favor + esse to be—more at PRO-, IS]

Syn proud, arrogant, haughty, lordly, insolent, overbearing, supercilious, disdainful mean showing scorn for inferiors. Proud may suggest an assumed superiority or loftiness but just as often implies strong self-respect or sense of accomplishment; arrogant implies a claiming for oneself more consideration or importance than is warranted . . . Webster's Dictionary

PHYSICIANS ARE proud people, as indeed they should be. For physicians have accomplished much and will continue to do so.

But too much pride may lead to arrogance.

Arrogance, according to the Oxford English Dictionary, is: the taking of too much upon oneself as one's right; the assertion of unwarrantable claims in respect of one's own importance; undue assumption of dignity, authority, or knowledge; aggressive conceit, presumption, or haughtiness. Is arrogance a trait of the medical profession? How does a physician persuade a patient to follow a course of therapy? Does he sit down with his client, discuss the anatomy, physiology, and pathology of the disease, the pharmacodynamics of the treatment? If he considers his patient an intellectual equal, theoretically this is the course he should pursue. His failure to do so is based partly upon the exigencies of time and partly upon his assumption that the patient, not having attended medical school, cannot understand.

But there is more to this problem than time and conceit. The wise physician wants to get the job done. He has a therapeutic regimen to impose upon his patient. Does he patiently explain the side effects and toxic effects of his projected drugs? If surgery is preferred, does he conscientiously describe the immediate morbidity, the early and late mortality, the complications, the failure rate; does he list these for his patient, reciting them like the ten plagues, so he can get an informed consent?

In the present climate of equating a bad result with malpractice, admittedly the wary surgeon will discuss untoward effects and may even include in the signed consent the list of potential tragedies that may follow his course of therapy. But he should understand that his patient pays little attention to the list of complications that might affect some one else but not him. The patient accepts the doctor mainly for reasons not related to statistics. He responds to a charade the doctor acts out: I am a skillful experienced doctor; I know what to do in your case; also I am your friend who will do you no harm; you can trust me to do the right thing: in a word—Arrogance.

The doctor-patient relationship fosters arrogance on the part of the physician. And this tendency increases as possible benefits and dangers of a given course of treatment increase, reaching its maximum therefore with surgery.

I recall a 19-year-old woman I saw when I was an intern at the Minneapolis General Hospital. Her story was classic: No period for ten weeks, right lower quadrant pain for two days and then evidence of anemia and shock. The cervix was blue, large, and tender. I suggested the diagnosis of tubal pregnancy (presented no doubt in a cocksure manner). She greeted this with disbelief and said pregnancy was out of the question. She refused to discuss surgery. My comments escalated quickly and ended with the advice that if she didn't permit surgery she'd go out in a box. And I then caught hell from my resident who told me that it took him three hours to undo the harm I had done by my "advice." He spent that time humbly gaining her confidence to the point where she would permit an "exploratory." Of course she did have an ectopic pregnancy and lived to leave the hospital but through no effort of mine. Scientific training and knowledge combined with a logical explanation (laced I am sure with the arrogance of an intern who "knew his stuff" and had just made a nice diagnosis) proved to be too weak a vehicle to move the patient to the correct treatment. The posture of arrogance must be concealed in the garb of humility.

The incessant adulation the physician receives from his patients often leads the doctor to the suspicion that probably the patients are accurate in their assessment: they think the physician is wonderful because he is a wonderful person. "First God and then the doctor." Too much of this and the doctor becomes insufferable. Failures help in correcting this attitude, especially failures presented before such juries as a weekly case conference. A bit of arrogance is a necessary part of our stock in trade. Certainly it is unavoidable when we have to make the fateful decisions the patient will not or cannot make himself.

But let us use it judiciously with balance—as a physician of another era, Doctor Arthur Conan Doyle, suggested in this passage:

> *"My dear Watson," said he, "I cannot agree with those who rank modesty among the virtues. To the logician all things should be seen exactly as they are, and to underestimate one's self is as much a departure from truth as to exaggerate one's own powers."*—Arthur Conan Doyle, "The Greek Interpreter," Memoirs of Sherlock Holmes, 1893.

Reuben Berman, M.D.
Editor Emeritus

Cerebellar Hemorrhage

THE DIAGNOSIS and management of cerebellar hemorrhage is a challenging subject, and Doctor Vincent's* article presents a superb review of the significance of cerebellar hemorrhage, including its clinical hallmarks, differential diagnosis, and current surgical management. He accurately emphasizes the fact that cerebellar hemorrhage is a true clinical emergency and that with prompt diagnosis and appropriate treatment, the end results may be quite satisfactory.

The computerized tomographic scan has added greatly to the diagnosis in this condition, but it should be recognized that the availability of this diagnostic test is still somewhat limited, especially under urgent circumstances. Because of the delays inherent in performing necessary diagnostic procedures and in arranging for surgery under optimum conditions, it is worthwhile to re-emphasize the acute management of patients who are decompensating from increased intracranial pressure. Currently, this consists of prompt endotracheal intubation and hyperventilation to pCO_2 levels of 30 to 34 mm. of mercury, administration of an osmotic diuretic (Mannitol, 1 to 2 gm. per kilogram i.v. given over 20 to 30 minutes), and the use of steroids (Decadron, 10 mg. i.v. as a loading dose and 4 mg. q. six hours subsequently). This mode of management may be lifesaving in cases of cerebellar hemorrhage in that it may help to provide the time necessary for diagnosis and therapy.

Edward R. Laws, Jr., M.D.
Rochester, Minnesota

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*See page 453.

Cold Thyroid Nodule

LUND AND SHAFER* present a brief review and an interesting case illustrating a facet of an entity more frequently and earlier detected since the widespread routine application of multichannel analyzers. Presentation of parathyroid adenoma as a neck mass surely is becoming less frequent, although a recent series indicates seven of its last sequential forty patients with parathyroid adenoma to have presented with neck mass as the chief complaint.[1] Deformity of the thyroid scan is certainly caused by such parathyroid adenomata; it is surprising to see that so few are recorded in the literature. The high incidence (one-third) of co-incidental association of parathyroid adenomata of all sizes and carcinoma of other organs has been recorded in the Memorial series and the fact that a relatively large number of these were thyroidal (five percent mixed papillary) is of particular interest in regard to thyroid scan findings and the difficulty of their interpretation.

Stanley C. Von Drashek, M.D.
Minneapolis, Minnesota

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*See page 448.

References

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Tennis Elbow

DR. JAMES D. PRIEST has summarized very thoroughly the factors involved in a rapidly increasing sport-related condition, tennis elbow. This condition is probably more commonly seen in non-tennis players as well. Conservative management is varied and the last resort is a surgical approach. His conservative regiment for treatment for the average tennis player is well founded and highly recommended.

Elmer R. Salovich, M.D.
Minneapolis, Minnesota

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*Page 367.

National Cooperative Gallstone Study

ABOUT 16 MILLION people in the United States have cholesterol gallstones. Gallstones form because bile contains more cholesterol than can be solubilized by the bile acids and lecithin present in the bile. Administration of chenodeoxycholic acid, a bile acid normally found in human bile, increases the cholesterol dissolving capacity of bile.

A number of small studies have indicated that chenodeoxycholic acid may be effective in dissolving cholesterol gallstones. However, a large controlled study is necessary to definitively establish the efficacy, safety, and optimal dosage level of chenodeoxycholic acid.

The National Institutes of Health (NIH) have approved initiation of a clinical trial of chenodeoxycholic acid for gallstone dissolution as part of the National Cooperative Gallstone Study (NCGS). Also, the Food and Drug Administration has allowed initiation of the clinical trial of chenodeoxycholic acid by the NCGS.

Ten NCGS Treatment Centers have been selected. They are: University of California, San Francisco; Yale University Medical School, New Haven, Connecticut; University of Minnesota, Minneapolis, Minnesota; Scott & White Memorial

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Hospital, Temple, Texas; The New York Hospital-Cornell Medical Center, New York; Emory University, Atlanta, Georgia; University of Pennsylvania Medical School, Philadelphia; Mayo Clinic, Rochester, Minnesota; Duke University Medical Center, Durham, North Carolina; and Cedars-Sinai Medical Center, Los Angeles, California.

One thousand patients (100 at each center) will be randomly allocated into three treatment groups. One group will receive a low dose of chenodeoxycholic acid (375 mg. per day) which has been shown to induce favorable changes in bile but which has not yet been tested in clinical trials for gallstone dissolution. A second group will receive a higher dose of chenodeoxycholic acid (750 mg. per day), a dose which from previous studies appears to be effective in gallstone dissolution. Finally, a control group will receive placebo (inactive capsule) and provide information on the natural history of untreated gallstone disease for comparison with the treated patients.

The criteria for admission of patients to the study are:

1. The presence of radiolucent gallstones in a gallbladder seen on a gallbladder Xray.

2. The patient is either female (postmenopausal post-tubal ligation, or posthysterectomy) or male between 21 and 70 years of age.

Exclusion criteria include excessive obesity (200% of ideal body weight), liver disease, inflammatory bowel disease, severe heart disease or malignancy.

All patients who are to be considered for inclusion in the study must be referred to a Treatment Center by their personal physician who will continue the general care of his patient while receiving periodic reports from the center of his patient's progress in the study.

The patients will be followed for two years with periodic examinations, blood tests, necessary Xrays, and duodenal drainage for determination of bile composition.

All expenses for examinations, tests, and treatment related to the experimental program will be covered by each Treatment Center. The expense of treatment for incidental illnesses unrelated to chenodeoxycholic acid therapy or for recognized complications of gallstone disease including cholecystectomy, however, will not be covered by the program. Booklets have been prepared for the referring physicians detailing the protocol of the NCGS.

Russell F. Hanson, M.D.*
Minneapolis, Minnesota
Johnson L. Thistle, M.D.†
Rochester, Minnesota

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*Director, University of Minnesota Treatment Center, Minneapolis, Minnesota.

†Director, Mayo Clinic Treatment Center, Rochester, Minnesota.

Courage Center

In December, 1972, the Minnesota Society for Crippled Children and Adults moved into its new headquarters at Courage Center, 3915 Golden Valley Road, Golden Valley, Minnesota 55422.

Courage Center is a comprehensive rehabilitation facility dedicated to serving physically handicapped children and adults from all over Minnesota. At Courage Center, emphasis is placed on recreation rehabilitation, and education.

The recreation program includes Camp Courage (located near Maple Lake, fifty miles west of Minneapolis), Courage North (located on Lake George, twenty miles south of Bemidji), Courage Day Camps in thirteen communities, and a variety of recreation programs at Courage Center.

The rehabilitation unit of Courage Center, now called Curative Services, was formerly the Minneapolis Curative Workshop. Basically, the programs offered are: therapeutic nursery school, speech and hearing services, physical and occupational therapy, parent education, social development, and work experience programs. All clients of Curative Services must be referred by a physician.

Courage Center is open from 8:00 a.m. to 4:30 p.m. Monday through Friday.

For information, please contact: Camping and Recreation—Jim Olson or Bob Polland (588-0811), Curative Services—Dolores Gillette (588-0811).

John Dumont
Courage Center

Letters to the Editor

Provider Agreements

Dear Editor:

Recently, we all received Provider Agreements from the Department of Public Welfare. These agreements require us to keep such records as are necessary to document services charged for, to provide such information to the State Agency upon request, and to comply with Title VI of the Civil Rights Act of 1964.

Some physicians in Ramsey County have mistakenly associated this Provider Agreement with Rule 47, and have also assumed that signing this Agreement will give the Department of Public Welfare the right to inspect the personal records of their patients. Both of these assumptions are wrong. The Provider Agreement, quite simply:

1) is required by the Federal Government. Title 45 Code of Federal Regulations, section 250.21 *requires* that a State plan for medical assistance under Title XIX *must* provide for such agreements with every person or institution providing services under the State plan. Failure of DPW to comply would mean no money for the providers or the state.

2) asks us to provide ledger cards or other proof of services rendered. We are asked to document the services for which we are being paid.

3) does not ask us to violate the Canons of Medical Ethics.

4) does not negate a long and well-documented guarantee of physician-patient privilege. For example, see: Jones on Evidence, 1972; Maas v. Laursen, 219 Minn. 461, 18 N W 2d 233 (1945); Minn. Stat. 595.02, subd. 4.

What this means to me is that a physician cannot release information to a third party without the consent of the patient. I cannot believe that the Department of Public Welfare would ever breach the rights of its clients and ask for privileged information; however, if such an occasion arose, we have ample legal precedent to defy such an effort.

James Janecek, M.D.
St. Paul, Minnesota

Biting Insects

Dear Editor:

Again this year I am compiling a Biting Insect Summary and would appreciate any case reports of unusual allergic reactions, especially systemic (sneezing, wheezing, urticaria) to bites of insects; i.e., mosquitoes, fleas, gnats, kissing bugs, bedbugs, chiggers, black flies, horseflies, sandflies, deerflies, etc.

I would like physicians to supply me with case reports of those patients who have had unusual reactions to such insects. Include in your reports the type of reactions (immediate and delayed symptoms), treatment, the age, sex, and race of the patient, the site of the bite(s), the season of the year, and any other associated allergies.

If skin tests and hyposensitization were instituted, I would like the report of both. Please note that it is the biting (not stinging) insect in which I am interested.

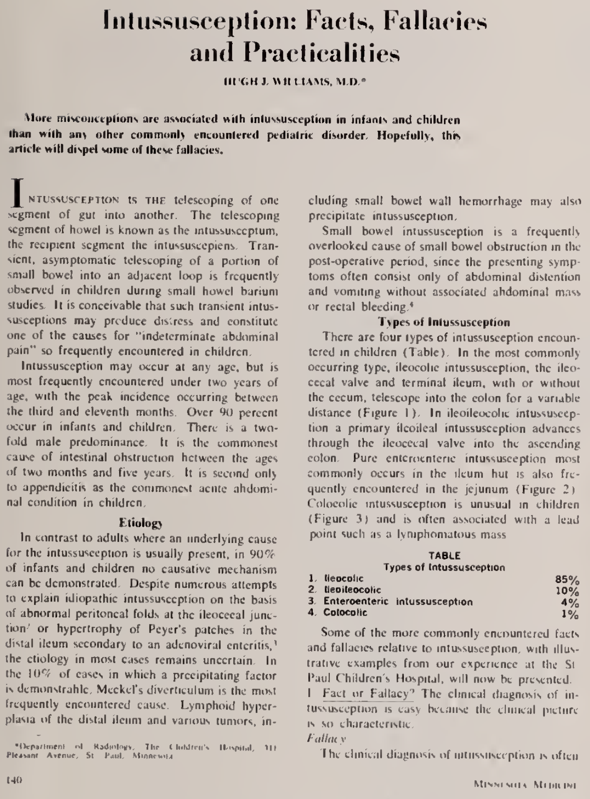
If you have found any insect repellent, local treatment, or insecticides of value, I would also appreciate this. Please send this information to the following address:

Claude A. Frazier, M.D.
4-C Doctors Park
Asheville, NC 28801

Claude A. Frazier, M.D.
Asheville, North Carolina

MINNESOTA MEDICINE Honor Awards

The Board of Editors announce the following best manuscript and best cover published in MINNESOTA MEDICINE during 1975.



Intussusception: Facts, Fallacies and Practicalities

HUGH J. WILLIAMS, M.D.*

More misconceptions are associated with intussusception in infants and children than with any other commonly encountered pediatric disorder. Hopefully, this article will dispel some of these fallacies.

INTUSSUSCEPTION IS THE telescoping of one segment of gut into another. The telescoping segment of bowel is known as the intussusceptum, the recipient segment the intussuscepiens. Transient, asymptomatic telescoping of a portion of small bowel into an adjacent loop is frequently observed in children during small bowel barium studies. It is conceivable that such transient intussusceptions may produce distress and constitute one of the causes for "indeterminate abdominal pain" so frequently encountered in children.

Intussusception may occur at any age, but is most frequently encountered under two years of age, with the peak incidence occurring between the third and eleventh months. Over 90 percent occur in infants and children. There is a twofold male predominance. It is the commonest cause of intestinal obstruction between the ages of two months and five years. It is second only to appendicitis as the commonest acute abdominal condition in children.

Etiology

In contrast to adults where an underlying cause for the intussusception is usually present, in 90% of infants and children no causative mechanism can be demonstrated. Despite numerous attempts to explain idiopathic intussusception on the basis of abnormal peritoneal folds at the ileocecal junction[2] or hypertrophy of Peyer's patches in the distal ileum secondary to an adenoviral enteritis,[3] the etiology in most cases remains uncertain. In the 10% of cases in which a precipitating factor is demonstrable, Meckel's diverticulum is the most frequently encountered cause. Lymphoid hyperplasia of the distal ileum and various tumors, including small bowel wall hemorrhage may also precipitate intussusception.

Small bowel intussusception is a frequently overlooked cause of small bowel obstruction in the post-operative period, since the presenting symptoms often consist only of abdominal distention and vomiting without associated abdominal mass or rectal bleeding.[4]

Types of Intussusception

There are four types of intussusception encountered in children (Table). In the most commonly occurring type, ileocolic intussusception, the ileocecal valve and terminal ileum, with or without the cecum, telescope into the colon for a variable distance (Figure 1). In ileoileocolic intussusception a primary ileoileal intussusception advances through the ileocecal valve into the ascending colon. Pure enteroenteric intussusception most commonly occurs in the ileum but is also frequently encountered in the jejunum (Figure 2). Colocolic intussusception is unusual in children (Figure 3) and is often associated with a lead point such as a lymphomatous mass.

TABLE
Types of Intussusception

1. Ileocolic	85%
2. Ileoileocolic	10%
3. Enteroenteric intussusception	4%
4. Colocolic	1%

Some of the more commonly encountered facts and fallacies relative to intussusception, with illustrative examples from our experience at the St Paul Children's Hospital, will now be presented.

I. Fact or Fallacy? The clinical diagnosis of intussusception is easy because the clinical picture is so characteristic.

Fallacy

The clinical diagnosis of intussusception is often

---

*Department of Radiology, The Children's Hospital, 311 Pleasant Avenue, St. Paul, Minnesota

140

MINNESOTA MEDICINE

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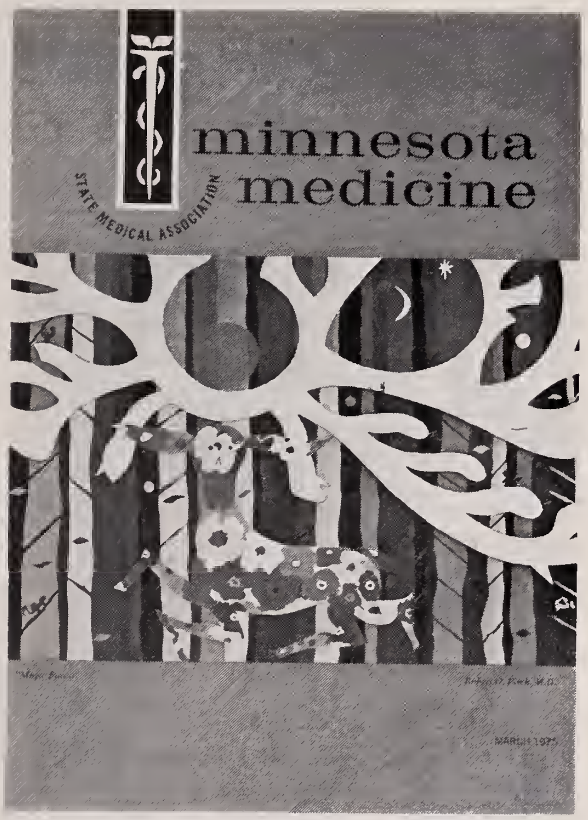

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Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

Warnings: Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I. reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

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* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. **Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

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Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

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Medical Library

LATCH

SHERRY A. HARGRAVE*

Although the concept of LATCH (*L*iterature *A*ttached *T*o *CH*arts) as a service of the hospital medical library was introduced several years ago, little has appeared in the literature on how it has worked. The medical library at North Memorial Medical Center in suburban Minneapolis initiated its LATCH service in the spring of 1974 with several modifications to meet the operational patterns and needs of a 550-bed private hospital.

LATCH was designed to function as part of the library's outreach program at the hospital, making clinical information available at the patient's bedside for one or more members of the health care team.

The LATCH service was organized to serve three primary groups of users (requesters):

. . . *Medical Services*—Requests for specific clinical information relating to diagnosis and treatment.

. . . *Nursing Services*—Requests for general clinical information relating to the disease and condition of the patient.

. . . *Ancillary Services*—Requests for specific therapeutic regimens recommended for the recovery and recuperation of the patient.

Operational features of the LATCH program were established after several months of experimenting. Procedures developed for the program are briefly discussed:

1. The completion of a LATCH Request Form available at each nursing station is the first step in initiating the program. The information requested on this form provides a topical outline of the kinds of information needed by the requester (Figure).
2. The nursing station attaches a copy of the LATCH Request Form to the patient's chart and calls the information into the library.
3. The library staff immediately completes a Modified LATCH Request Form specifying subject headings and search strategies for manual or computer retrieval of the information desired.
4. The retrieved information is assembled.
5. The requester personally visits the library to review and select appropriate material for attachment to the patient's chart. Information requested for chart attachment must be approved by the attending physician.
6. Selected articles and/or excerpts are photocopied and distributed to the nursing station with a cover sheet identifying the patient for which the LATCH information was retrieved.
7. The LATCH material remains attached to the patient's chart until discharge. The requester or the nursing station then decides either to retain or discard the LATCH material.
8. The library's recording and retrieval system for the LATCH program includes: (A) card catalog entries for LATCH bibliographies, (B) entry of attachment material citations in a logbook and (C) a reference index by last name of LATCH requester.

Latch Request Form

Requester's name: .... Floor: .... Date: ....

Person calling library, if different than requester: .... Date: ....

Medical staff and resident on case: ....

Patient's name: .... Age: .... Rm & Bed: ....

Date of admission .... Expected discharge: ....

Subject: ....

Specifically relating to (e.g., diagnosis, treatment, etc.): ....

For whose information is the material primarily intended: (e.g., nurses, doctors, both or others) ....

Qualifications of the subject matter in relation to the patient, when applicable (e.g., part of the body or organ involved, treatment being given to the patient, etc.):

....

Comments: ....

---

*Director, of Medical Library Services, North Memorial Center, Minneapolis.

Present usage of the LATCH service averages five requests per month. This represents approximately ten percent of the total literature searches completed by the library. In the future, the library staff anticipates increased usage of LATCH through orientation meetings and an intensified publicity program. Currently, a study of the operation of LATCH at the nursing stations is in progress.

The LATCH program provides opportunity for the library staff to make a direct contribution to patient care. With continued evaluation and improvement, LATCH is perceived as the foundation from which additional medical library outreach programs will be developed at North Memorial Medical Center.

Request for Physician's Art Work

For many years the Board of Editors of MINNESOTA MEDICINE has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers have received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Pictures will be returned if identified with the name and address of the physician. Please submit your picture as prospective cover subjects to the Editor of MINNESOTA MEDICINE, 101 East 5th St., St. Paul, Minnesota 55101.

During 1976 the Editors would like to pay homage to the Bicentennial by having our covers depict places, events, scenes, etc., that have historical or patriotic significance for the State of Minnesota. Please keep the Bicentennial theme in mind when submitting prospective covers for 1976.

Farrell Stiegler, M.D.
Cover Editor

Minnesota Heart Association

Dr. Brian Campion of St. Paul has been elected president of the Minnesota Heart Association. and Dr. James Kenney of Minneapolis is the newly elected chairman of the board.

Drs. Carlos Harrison, George Gura, P. J. Osmundson and Ralph Spiekerman of the Mayo Clinic were re-elected to the board. Newly-elected to the board from the Mayo Clinic were: Drs. Roger White, Hugh Smith, and Charles O'Brien.

History

Hessian Troops in the American Revolution

Their Medical and Medicinal Care[*]

RUDOLF SCHMITZ, Ph.D.[*][†]

THE GERMAN PHYSICIAN—botanist Johann David Schoepf (1759-1800) reported this anecdote from "Free North America": "A group of Hessians, on encountering a row of buckwheat sheaves spent half an hour bravely firing at the enemy without causing them to move an inch. The farmers of the region seized the opportunity to label the German troops "blind Hessians."

To this day the deployment of Hessian mercenaries overseas, loaned to the British Crown by their own ruler, Friedrich II, Landgrave of Hesse-Kassel, has embarrassed historians in Germany and abroad. In the light of recent international engagements, the lot of the much maligned mercenaries who were fighting "the wrong war, the wrong people and at the wrong time" deserves a more detached evaluation. In Germany the familiar saying "Ab nach Kassel" ("Off to Kassel") still means condemning somebody to an uncertain fate against his will.

Treaties

The practice of hiring out mercenaries had been used by the Landgraves of Hesse-Kassel for almost 140 years. Hessian troops, on the basis of "treaties," fought for many European rulers on almost all battlefields between 1677 and 1815, including service under the Duke of Wellington against Napoleon as their last mercenary engagement.

By the British-Hessian subsidiary treaty of January 15, 1776, a total of 13,976 men were placed at the disposal of the British crown for deployment on the American continent, a large force, even by today's standards. The two Hessian Corps, as demanded by tradition and treaty, operated independently throughout the war. These Corps had autonomous medical services. Article XII of the treaty states: "Sick members of the Hessian Corps shall remain under the care of their physicians, surgeons and other persons appointed for that purpose under the orders of the general commanding the corps of that nation, and everything shall be allowed them that His Brittonic Majesty allows his own troops."

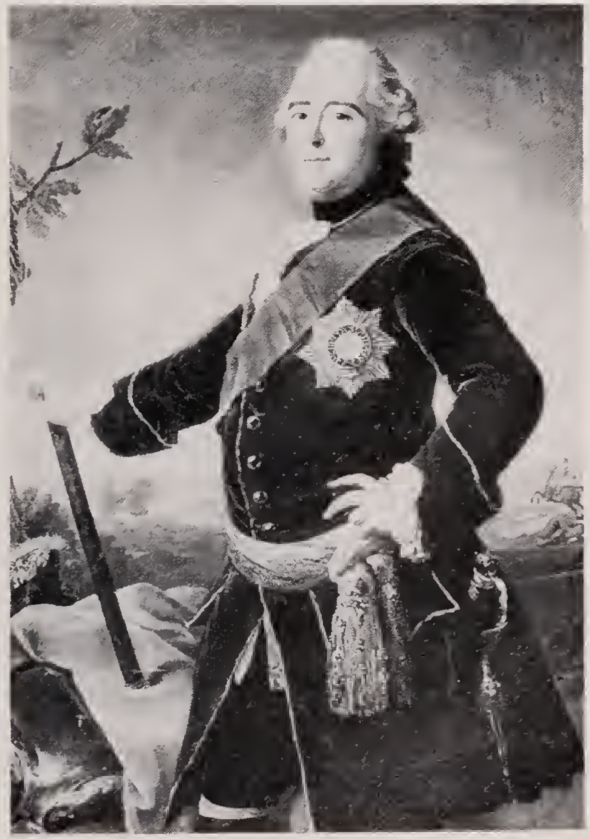

Fig. 1—Landgrave Friedrich II of Hesse-Kassel.

EDITORIAL NOTE: To commemorate the Bicentennial, MINNESOTA MEDICINE is publishing a series of historical articles. This is the first such article. These papers will concern Medicine in the American Revolution or Minnesota's role in Medicine the last 200 years. This article tells the medical woes of Hessian mercenaries hired by the British to fight Americans. I would like to thank Doctor H. W. Heupel of Minneapolis, who, after hearing Doctor Schmitz present this paper at the University of Minnesota, solicited the manuscript and edited it.

[*] Part of a guest lecture given on April 16, 1976, at the School of Pharmacy, University of Minnesota.

[†] Professor and Head, Institute of History of Pharmacy, Philipp's University, Marburg/L, Federal Republic of Germany.

Medical and Apothecary Personnel

Several years earlier, the Landgrave had issued extensive medical regulations for his principality, dealing with training of personnel in detail, but he had failed to consider the military aspects altogether. Thus our information stems from indirect sources: casualty lists, payroll and financial records, and "size and assignment" rosters. The latter lists the soldiers by their height, a factor of military importance two centuries ago. The records, stored in the Hessian State Archives in Marburg, provide us, aided by computer analysis, with detailed information of all Hessian soldiers in America.

The professional qualifications of the medical and paramedical personnel of the Hessian Corps were woefully low—certainly not the best Europe had to offer at the time. A regimental field surgeon, 49 years old, had joined the corps at age 17: a self taught man. A 19 year old musketeer found himself promoted to "company field surgeon." Promotions from private soldier to field surgeon were quite common. Another private was transferred from Germany in 1780 "to serve as an apothecary with the Hessian troops."

The treaty of 1776 mentions 100 "field surgeons" but no field hospital or dispensary personnel. Three graduate physicians and three field apothecaries are listed. One apothecary was promoted from journeyman in 1778, and another apothecary-journeyman is mentioned for 1778 and 1779. Two chief surgeons and six "ordinary surgeons" are named as working in field hospitals. The esteem in which these professionals were held is reflected in their pay: The physician tops the list, followed at some distance by the field surgeon. The apothecary ranks sixth with a monthly pay of £3, 6 s, 8 d, below the field hospital clerk, but ahead of the cook. The apothecary's journeyman is second to last with £2 per month, ahead of the hospital orderly.

Medical Budget

If the payroll seems meager, so is the amount spent on medical supplies for the entire expeditionary force: £677 in 1777, £519 in 1778 and £746 in 1779. During these years medicaments for £144, £89 and £144 were charged to "superior officers and other persons."* The Hessian battalions also drew 80 to 100 marks annually for stocking their field medicine chests. In general, medicines were supplied free to both the English and Hessian units. Officers, though, were expected to pay for their personal medical needs. General Von Knyphausen, in a report to the Landgrave complained that this custom led his officers to neglect their health and argued that medicaments should be dispensed free of charge to the officers, as they were provided free by the British Crown.

One Regiment's Experience

For a closer look we selected the Von Ditfurth

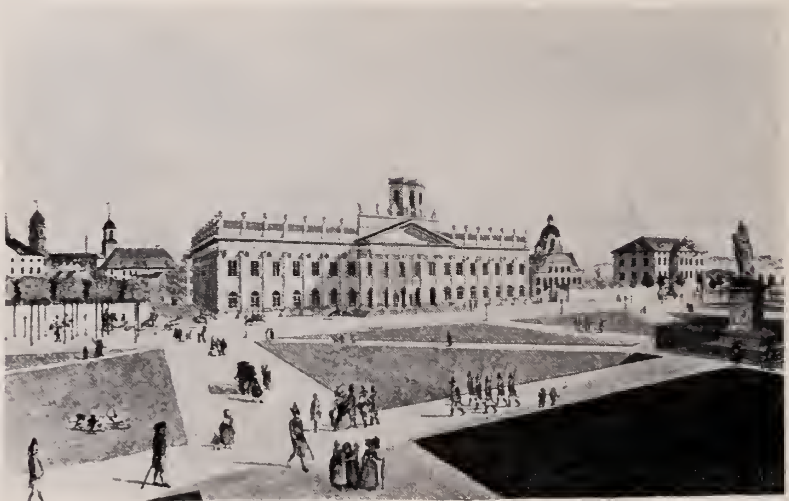

Fig. 2—Earnings from mercenaries provided the funds for magnificent parks and palaces in Kassel. Friedrichsplatz, around 1780.

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*Editor's note: The suspicious reader wonders who and how lovely "other persons" were. HWH.

Regiment, which had it's home garrison in Marburg. It left on February 11, 1776 for the North Sea port of Bremerlehe, where it embarked after a journey by foot and by river, on March 23, 1776. On August 15, 1776 it landed at Staten Island. This regiment of 633 comprised 21 officers, 60 noncommissioned officers, five field surgeons, 22 bandsmen and 525 privates. The losses at sea, in spite of the long and cumbersome crossing were low: four fusiliers (riflemen) died in 1776, one recruit was reported missing at sea in 1780 and it is stated of another that "because of an attack of melancholy he threw himself into the water at Charleston and drowned." Another fusilier died at sea as the result of an accident in 1783.

After arriving on the new continent the number of the sick increased from month to month: 38 illnesses are reported for August 1776 and a steep increase to 82 for the month of December, representing 12 percent of the troop strength. In the following two years the regiment had between 10 and 30 men sick at any given time, but their number swelled to 158 in October of 1780 and 33 died. In that year the regiment had been transferred from New York to Charleston, South Carolina, where it went into action. Malaria and other epidemics took their toll, outweighing battle casualties by far. In August of 1782 alone, 224 soldiers became sick and 10 died, leaving one third of the regiment unfit for action. In July of 1783, the last month before returning to Europe, the regiment listed 64 men sick. While 210 men died from disease, only five were killed in action and three succumbed to wounds later.

None of the casualties occurred in historic battles. Two men were killed "while pursuing rebels," one was "shot dead by the enemy, on command near Thomson's house in South Carolina," another fell in Juda Spring, and the fifth was killed "by a refugee on James Island." Many of the deaths were caused by the hot climate to which the Hessians were unaccustomed. In the hot summer of 1781 a corporal, a carrier and a private reportedly died of "extreme heat" on the way from Charleston to Shubricks, and another corporal died "suddenly" en route from Charleston to Dorchester.

Hospital Ships

Morale was low and at times the whole unit was unfit for action. The care of the sick and wounded was left to field hospitals in the garrisons and to two hospital ships which were placed along the coast. The hospital ship "Eleanora" rode at anchor off Newport and the British ship "Three Sisters" off the coast of South Carolina. The latter ship was made available to the Hessians during December 1782 and January 1783. Five fusiliers and one corporal died on it. These ships were converted troop carriers, ill fitted for the care of the sick. Major Baurmeister, Adjutant General of the Hessian troops noted in his diary: "These miserable hospital ships have killed many of our soldiers. Of five sick in my company only

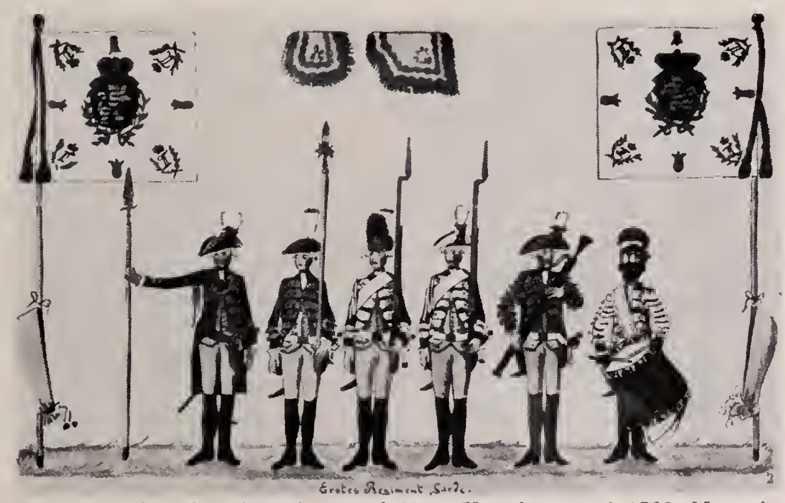

Fig. 3—First Guard Regiment of Hesse-Kassel, around 1780. Note the two musicians. No match for Yankee guerrillas.

one has recovered."

Hospitals and Supplies

The permanent field hospitals performed better. Adherence to hygiene and the new practice of vaccination helped to reduce illnesses after the disastrous experience of 1781 and 1782. Still, the death rate rose during the winters in the unheated field hospitals. Medicines and food were in short supply. An entry in the Journal of the Hessian Corps reads: "Because of the almost complete lack of medical supplies and the awful increase in the price of food, the care of the sick and wounded has been inadequate from the very beginning." More telling is a note in the diary of a Hessian captain after the surrender of Yorktown: "Our poor sick and wounded lay without medication or food, in conditions pitiful enough to soften the hardest heart. These wretched fellows are dying like flies."

The Balance

Hessian casualties in America were high: 4626 men dead from illnesses and 357 killed in action. Their inadequate medical and medicinal care conveys a feeling of helplessness and resignation and probably contributed to the large number of Hessian soldiers taken prisoner (8029), deserting (2949) or "dismissed" (914). The paucity of battle casualties tends to confirm the notion of the Hessian general Von Ochs that all the battles fought in North America were really "serious skirmishes."

Nonwithstanding, the general's opinion, it makes the losses resulting from poor medical and medicinal care all the more regrettable.

Mayo Physician Elected to Head National Group

Dr. John Hill, senior consultant in proctology at Mayo Clinic, has been elected president of the American Society of Colon and Rectal Surgeons at its annual meeting in New Orleans.

Dr. Hill is editor of the society's journal, Disease of the Colon and Rectum.

He came to Rochester in 1939 as a Mayo Graduate School resident and joined the Clinic staff in 1946 after serving with the Army in World War II.

He is a native of Ohio and earned his MD in 1933 from Ohio State University Medical School.

Clinical Path Conference

Fatal Iron Poisoning in a Pregnant Female

Case Report

ROBERT L. STROM, M.D.;[*] PHILIP SCHILLER, M.D.[†] ASA E. SEEDS, M.D.[†]
and ROBERT TEN BENSEL, M.D.[‡]

Case Report

Dr. Philip Schiller:

The patient was a 17-year-old white female, whose last menstrual period was four months prior to admission to Hennepin County General Hospital. The patient had ingested about 95 tablets of FER-IN-SOL[#] on November 3, 1973 in an apparent suicide attempt because of marital problems. She presented to the Emergency Room one hour later and was given syrup of Ipecac with good results. Partially digested iron capsules were seen in the vomitus. She vomited persistently and developed diarrhea.

Physical Examination

Blood pressure 150/110, pulse 110, respirations 16, temperature 98.6. She was a young woman in no evidence of distress, but occasionally vomiting dark material. The heart tones were normal. There was a grade I systolic murmur at the apex. The lungs were clear. There was mild epigastric tenderness and slightly hypoactive bowel sounds. A pregnant uterus was palpated, and the fundus appeared consistent with the gestational age of four months. Neurologic examination revealed decreased reflexes. The urine shortly after admission was described as "coke" colored.

Laboratory Studies

Hemoglobin 15.3 grams %, hematocrit 45, white blood cell count 20,500 with a normal differential. Serum sodium 134 mEq/L, serum potassium 4 mEq/L, serum chloride 103 mEq/L, CO_2 12 mEq/L. Blood glucose 353 mg.%, blood urea nitrogen 18 mg.%, prothrombin time 11.9 seconds, partial thromboplastin time 34.9 seconds. Blood gas studies revealed a pH of 7.31, and a pO_2 of 109 mm. of mercury. A serum iron subsequently determined was 1700 ugm.

Hospital Course

It was decided not to treat the patient with desferoxamine because of potential toxicity to the fetus. Bed rest and intravenous fluids were initiated. The emesis was Guaiac positive. The urine was dark brown, and the patient was oliguric. By the morning following admission the urine output had pregressively decreased to the point she was anuric. She was hypotensive and had a pulse of 136 per minute.

Laboratory studies showed a hemoglobin of 11.6 gm. %, white blood cell count 30,500 per cubic mm., blood urea nitrogen was 30 mg. %, and the blood sugar was 25 mg. %. Coagulation studies revealed a prothrombin time of 19.8 seconds and a partial thromboplastin time of 51.2 seconds. Urinalysis was positive for glucose, five to ten red blood cells and four to six white blood cells were present in the sediment.

The hospital course was one of continued acidosis, gastro-intestinal bleeding, hypoglycemia, and anuria. Treatment consisted of sodium bicarbonate and 50% dextrose given intravenously. A G.I. consultant recommended aggressive therapy to include exchange transfusion, renal dialysis, and possible use of desferoxamine.

The patient continued to show tachypnea, tachycardia, minimal urine output, and a blood pressure of 150/50. An exchange transfusion with 20 units of blood was undertaken. Fresh frozen plasma was also given. Desferoxamine was contraindicated because of acute renal failure. The evening of the second day she appeared improved, but she persistently had a low blood sugar of 40 mg. % and a bicarbonate of 11 mEq/L, despite intravenous sodium bicarbonate and dextrose. She remained oliguric. Her vital signs stabilized and the fetus spontaneously aborted. The coagulation times remained prolonged and platelet studies were markedly decreased. A consulting hematologist suggested the abnormal coagulation results were due to exchange transfusion with ACD blood, liver damage, G.I. bleeding, and dialysis. The patient was lethargic, confused and nasogastric drainage and stools were persistently Guaiac positive. Hypoglycemia, anuria, hepatic failure, blood coagulopathy and acidosis persisted. By the third hospital day there was decreased sensorium and increased rigidity. A chest Xray showed pronounced pulmonary edema. The patient was febrile with respiratory irregularity and hypotension, requiring Levophed. The patient expired on the third hospital day.

Dr. Rafael F. Valle:

Thank you, Dr. Schiller. We are fortunate to have Dr. Asa F. Seeds from the University of Minnesota, Department of Obstetrics and Gynecology to discuss factors related to placental permeability.

Dr. Asa Seeds:

As an obstetrician, it is unusual to face a situation where the mother has ingested an iron overdose. Our problem is that we have trouble getting enough iron into the systemic circulation through the oral route. We generally think in terms of a mucosal block to iron absorption and a limit even in the presence of anemia to the amount of iron that can be absorbed through the intestinal mucosa with excessive iron intake.

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[†] OB-GYN Department, University of Minnesota Hospital, Minneapolis.

[‡] Department of Pediatrics & Public Health, University of Minnesota Hospital, Minneapolis.

[#] Contents of elemental iron.

The unusual complications encountered here following maternal overdose of iron are rare. With respect to placental permeability, I think a few important concepts should be mentioned. Where the mother has high levels of serum iron, high enough to be life-threatening, you are primarily concerned with saving the mother's life. Under these circumstances, you really shouldn't worry too much about drug effects on the fetus and go ahead and treat the mother with whatever is indicated. You go ahead and treat the mother with whatever it takes to cure her problem, and concern yourself with the fetus only after you have taken care of the mother's situation.

In addition to that general concept, let's consider the two agents used here, iron and desferoxamine. Clearly, rather than being concerned about the desferoxamine crossing the placenta and harming the fetus, we should have been more worried about toxic fetal effects resulting from high maternal serum iron levels. The toxicity of desferoxamine is based upon FDA studies where animal species had some skeletal anomalies due to a dosage of desferoxamine slightly higher than the dosage used in humans. I have been unable to find a published reference for this to date other than the package insert, and I am not certain how significant this problem is. Desferoxamine has a molecular weight of 560 and is a highly charged ion with four hydoxal groups. You may infer from such physico-chemical properties that this compound will cross the placenta very slowly, if at all.

Even though it is a charged cation, iron crosses the placenta rapidly. The placenta is not going to protect the fetus from lethal levels of iron in the maternal circulation. I will be interested to hear if the fetus showed damage to the fetal liver or kidneys, because you have to suspect that even if you got the mother over this acute episode, you would have trouble with the baby from iron toxicity. Therefore, one might expect that rapidly transferred iron would harm the fetus, while the desferoxamine crossing only very slowly to the fetus not only presents no hazard, but may be of great advantage to the fetus as a chelating agent lowering iron concentration.

Dr. Valle:

Dr. Strom will present the pathology and afterwards, Dr. Schiller will comment on the pathophysiology of iron intoxication.

Dr. Robert Strom:

There is a paucity of literature on the pathologic findings of acute iron intoxication and what is available usually reports on fatal cases involving children. Most often, children ingest elemental iron thinking it is candy. I found nothing at all describing the pathologic changes in a young pregnant female.

At autopsy examination, she was an obese, young, white female. She had a Scribner shunt in the left forearm. There was pleural fluid in each chest cavity and about 50 cc. of bile-stained fluid in the pericardium. The heart weighed 275 grams and there was evidence of subendocardial hemorrhage involving the left ventricular side of the interventricular septum. There was also evidence of hemorrhage in the wall of the myocardium itself with a cellular exudation of PMNs due to increased capillary permeability. Apparently

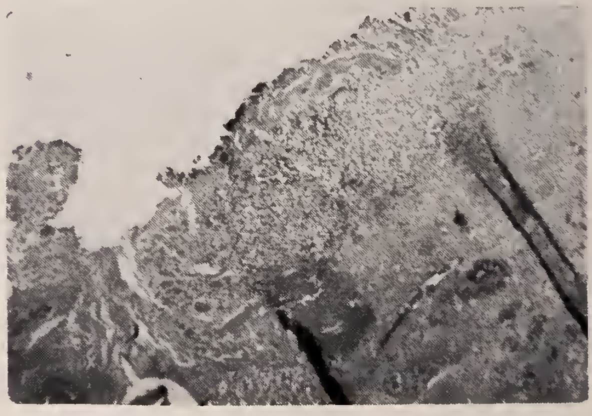

Fig. 1—Acute ulcer of the esophagus 100X.

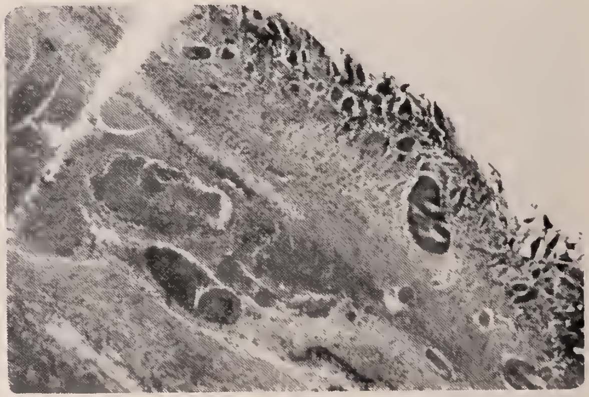

Fig. 2—Acute hemorrhagic ulcer of the stomach 100X.

there were signs of congestion on the chest Xray and our studies of the lungs suggest that this was due to intraalveolar hemorrhage.

The real shock organs for iron ingestion are the gastro-intestinal tract and the liver. This is a section taken through several ulcerated areas in the distal esophagus (Figure 1). You will notice there is marked dilatation of the submucosal vessels, and there is a heavy infiltration of polymorphonuclear leukocytes and evidence of esophageal erosion. This represents sections taken from the stomach, there being several small areas of hemorrhage in the submucosa (Figure 2). Again, we see vessel dilatation and necrosis of the mucosa. These ulcerations sometime proceed, in cases of chronic iron ingestion, and cause scarring and gastric outlet obstruction. The circulation is generally open to the ionic iron.

Looking at the liver we can see best on the cut section a pattern of hemorrhage outlining the hepatic lobules and the consistency of the liver was described as gelatinous. As we look at the liver findings, they are highly variable in several of the sections that we have of the liver. In areas of the liver the hepatocytes appear well preserved, but elsewhere periportal areas show little hepatic damage. The central areas show minimal alteration and brown pigment is localized around the central veins. Turning now to the areas of liver that were more severely involved, we can see zones of necrosis around the portal areas outlining separate lobules. The portal area appears to be the area of insult similar to the change seen in acute phosphorus poisoning. Here again, we can see an outline of the central vein and the hepatic lobules with zones of necrosis in the portal areas (Figure 3). In areas, the liver has undergone total necrosis and the sinusoid pattern is totally disrupted. The liver in these areas underwent total necrosis, and only a few residual bile ductules were seen. A reticulum stain shows preservation of the reticulum fibers around the sinusoids. Iron stains of this liver, interestingly enough, showed no evidence of iron with the Prussian blue stain.

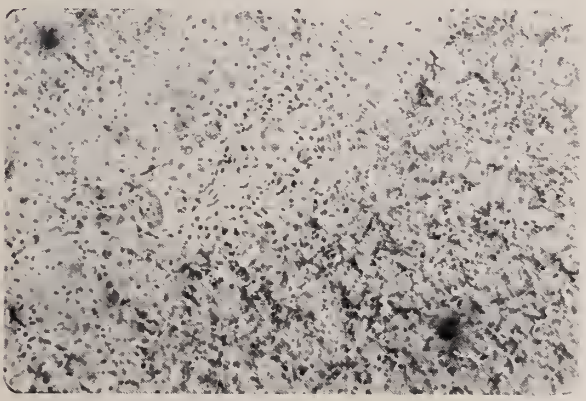
Fig. 3—Acute toxic liver necrosis 450X.

The kidneys were normal in size and the cortex appeared slightly pale. The microscopic observations in the renal cortex are remarkably normal in spite of the renal insult. There is slight vessel dilatation in the glomeruli and the tubules are well preserved. There was evidence of hemorrhage along the pelvis and in the renal pyramids. There was also evidence of dilation of vasa recta in the collecting system of the renal medulla and brown hemoglobin casts were seen in increased numbers. The iron stain of the kidney again showed no evidence of iron staining on the Prussian blue stain.

The uterus was, of course, enlarged and the endometrium was hemorrhagic. This is a section taken through the endometrium of the uterus, and there is no evidence of inflammation or abnormality. I think these changes in the endometrium would be consistent with a recently aborted pregnancy.

I reviewed the surgical pathology report on the fetus, and the fetus and placenta looked normal. Examination of the internal organs showed no definite pathologic alterations. In this section through the placenta we can see some PMN infiltration and areas of hemorrhage but no evidence of infarction. One of the sections seen from the fetus was fetal heart. There is evidence of minimal microscopic necrosis of cardiac myocytes without cellular reaction. Iron stains of fetal tissue did not show increased elemental iron to the Prussian blue stain.

Dr. Thomas Marubbio:

Were there any pathologic changes in the pancreas?

Dr. Strom:

The pancreas showed essentially nothing.

Dr. Philip Schiller:

I would like to discuss briefly the pathophysiology of acute iron poisoning. First, a few comments about normal physiology: the diet of an average adult contains 10-15 mg. of elemental iron per day, of which approximately one-tenth or 1.5

mg. is actually absorbed. In the past it has been considered that only small quantities of iron could be absorbed via the gastro-intestinal tract, that a mucosal block prevented excessive iron absorption. The fact that in acute iron poisoning, exceptionally large quantities of iron are absorbed (through an intestinal mucosa frequently found to be intact) disputes this view. The human body has no adjustable mechanism to compensate for iron overload.

In normal adults, only one-half the 1.5 mg. is excreted in the urine; this is not significantly increased in cases of acute or chronic iron overload. Iron is absorbed in a ferrous form, converted to the ferric form, and is then picked up by transferrin, an iron binding protein. The normal serum iron level is 70-150 micrograms %; the total iron binding capacity (reflecting the amount of transferrin available) is 300-400 micrograms %. When this level is exceeded, a small amount of circulating iron attaches to albumin and the remainder circulates in the free form. Presumably, toxicity is produced by the free or unbound iron. The average lethal dose of iron for humans has been estimated to be approximately 200 to 250 mg. of iron/kilogram of body weight. This represents about sixty 5-grain ferrous sulfate tablets for the average two year old. However, as few as ten such tablets have been fatal for a young child.

On the basis of animal studies and clinical experience, the major pathophysiologic findings in acute iron intoxication are: (1) hemorrhagic necrosis of the G.I. tract, (2) metabolic acidosis, (3) a coagulation disorder, (4) hepatic damage and (most importantly) (5) shock. Hemorrhagic necrosis of the gastro-intestinal tract usually results from the caustic stringent effect of iron. The extent of the mucosal damage is highly variable, but a functional disturbance is almost universally present. It is manifested by vomiting and diarrhea, both frequently bloody.

Metabolic acidosis is a prominent and consistent feature in experimental iron poisoning. This is likely true in most human cases, though many of the case reports do not include acid-base data. The acidosis is felt to be the result of two or three factors: (1) the conversion of large amounts of ferrous iron to ferric iron liberating an abundance of hydrogen ions or (2) an accumulation of organic acids because of anaerobic metabolism and shock or (3) possibly a direct interference in the Kreb's cycle by iron, leading to an accumulation of lactate and citrate.

Coagulation disorders have been noted in dogs and there have been scattered reports of apparent coagulopathies in humans. The patient we presented today showed significant alteration of her coagulation parameters. These changes occurred even before iatrogenic factors (such as the 20 unit exchange transfusion) could be implicated.

Hepatic damage has been inconsistently seen clinically, but histologically some degree of hepatic necrosis is frequently present.

Finally, we come to the most significant feature in acute iron intoxication—vasomotor collapse or shock. The clinical picture of shock is found in all fatal human and animal cases. Initially there is hemoconcentration and decreased plasma volume likely explained by a shift of fluid from the vascular compartment to the intracellular space. Blood pressure is initially quite variable but a progressively decreasing cardiac output and increasing pulse rate are noted. Hypotension invariably ensues. Marked capillary congestion and increased capillary permeability are consistent autopsy findings, accounting for the diminished venous return and decrease in cardiac output. It has not been shown whether this capillary dilatation is the result of metabolic acidosis or if iron itself directly affects the capillary bed.

Clinically, the patient ingesting an overdose of iron may proceed through four stages. The first stage lasts about six hours after ingestion. Bloody vomiting and diarrhea are frequently noted. Shortly thereafter, there may be shock, tachypnea and metabolic acidosis. Lethargy and coma may be present and death may occur at this time. The second stage, occurring from about six to 24 hours after ingestion, is one of transient improvement. During this phase the physician may be deceived into thinking that the patient is recovering. In the third stage, from 24 to 48 hours after ingestion, shock and metabolic acidosis are frequently seen. Leukocytosis, coma, fever, and convulsions may be present and death may occur at this time.

There is a fourth stage described in the literature that occurs (variably), consisting of gastrointestinal obstruction secondary to scarring which may be seen one to two months following ingestion if the patient survives.

Dr. Valle:

Next I would like to introduce Dr. Robert ten Bensel who is Professor of Pediatrics and Public

Health at the University of Minnesota Hospitals. He has been very much interested in the problem of iron intoxication as it occurs in children.

Dr. Robert ten Bensel:

I have no special expertise in iron poisoning except that as a pediatrician we are frequently involved in acute poisonings in children. The literature largely deals with children and I was only able to find one case that was well documented in the adult literature. I did look at the cases in this hospital between 1968 and 1972. There were ten cases admitted during this time, of which eight were children. The children were all between the ages of one and two and a half years of age. There have been two other cases in adults. One was a 17-year-old who ingested an unknown amount of iron. She was seen in the emergency room, emesis was induced by Ipecac, and she was admitted for observation after iron studies were drawn. The other patient was an 18-year-old who was pregnant and ingested her iron supplementation. No serum iron or total iron binding capacity was drawn. Both of these cases were admitted to the hospital for observation and there was no serious outcome.

We might look at the problem of iron poisoning in terms of what we call primary prevention and secondary prevention. Let's look at secondary prevention first; that is to say, what happened to this patient after the ingestion. Could this patient have been saved?

Elemental iron is rarely given to children in tablets or capsules. The 300 mg. ferrous sulfate tablets is the major iron compound that is available on the obstetrical service and ferrous sulfate liquid (13 mg/cc) is available for children. The liquid primarily damages the stomach and the duodenum whereas there is a tendency for the tablets to travel through to the lower intestinal tract. Thus, there is a difference in the pathology observed. Sometimes the iron tablets can be carried quite a ways down the G.I. tract. The important thing to remember is that iron is rapidly absorbed so the immediate treatment is critical.

The initial phase is critical for it may be very short, often as short as 30 minutes. In this case, according to my calculation, 28.5 grams of iron were ingested. This is a significant dose and it is important to know this on admission since the serum iron rises very rapidly. This case represents the natural history of iron poisoning. It is unfortunate many things were done late rather than early. What was seen in this case was vomiting and diarrhea, gradual improvement, and then shock and death in the third phase.

Returning to the question of secondary prevention—how can we intervene? What I wish to leave with you is a protocol to approach this problem in case you see this type of problem again. The key, once the patient has taken the iron, is to get it out. It has to be rapid. Emesis is best, ipecac is the most effective; 50% better than lavage. Apomorphine can be used. It works by direct action on the vomiting center. It is effective but the patient has to be observed very closely. An important factor with apomorphine is that the stomach has to be full because you can rupture the stomach due to violent vomiting. It used to be used in our emergency room but it has been discontinued for several reasons. You have to have the antedote Naline immediately available and give it promptly after the patient begins vomiting. Therefore, you have to sit with the patient and wait for him to vomit. Copper sulfate was used in this hospital for a long time to induce emesis. This has a direct irritant effect on the gastric mucosa thus inducing vomiting. Copper sulfate is itself a poison and it has to be removed if the patient doesn't vomit. Syrup of Ipecac is, therefore, the treatment of choice. The dose for a 17-year-old would be two to three tablespoons. Generally, about 15 cc. is given to one year and an ounce over two.

Physician in the Audience: What is the difference between the syrup and the elixir of Ipecac?

Dr. ten Bensel:

The elixir of Ipecac is about twenty times stronger and in itself is highly toxic. This is a very important point, because there have been mixups using Ipecac and not knowing the difference between syrup and elixir.

Lavage is recommended if there is coma. In this case where you know a large quantity of iron tablets were ingested, I would advise lavaging with 5% sodium bicarbonate. This keeps iron in a reduced form. It is recommended that if there is blood found in the stomach at the time of the initial lavage, to leave the sodium bicarbonate in the stomach to prevent the oxidation of iron.

A flat plate of the abdomen is helpful. Iron is radio-opaque and it can be seen on the flat plate of the abdomen. Sometimes you have to lavage several times to be sure you get all the iron. Tablet or capsules can adhere to the side of the gastro-intestinal lining and the Xray can tell you if all the iron is removed. The Xray can also identify if there are tablets further down in the gastro-intestinal tract; enemas may be indicated.

Consideration of administration of desferoxamine then becomes important. In children, we usually give the desferoxamine orally but it is unproven whether it has much effect in binding the iron and carrying it out of the gastro-intestinal tract. One of the tests that is used is to give desferoxamine and if the patient urinates an orange-colored urine that means that it is binding iron. Other studies suggest that once iron is bond to desferoxamine, it is not absorbed from the gastrointestinal tract.

An emergency serum iron is essential in the initial management of iron poisoning. If the serum iron is high, vigorous treatment is required.

Dr. Schiller:

One of the authors who works for the Ciba Company which makes desferoxamine, found that if the initial serum iron is 500 mcg. %, less than 10% of these people will have symptoms of coma or shock. But if it exceeds 1000 mcg. %, a high percentage of these people will go into coma and die. Therefore, the initial iron level drawn after iron absorption is extremely helpful in determining how aggressive to be.

Dr. ten Bensel:

Without the serum iron you are really left in limbo in making a clinical judgment.

Dr. Marubbio:

One of the problems in this case is that long before she went into shock she had increased serum amylase levels without renal failure. This led us to feel clinically that she had pancreatic damage.

Dr. ten Bensel:

The question is does the high amylase level and pancreatic involvement occur in children? This is something in this case where the pathology doesn't fit because there was no evidence of pancreatic damage at autopsy.

Dr. Strom:

The high amylase might be from bowel necrosis alone without pancreatic damage.

Dr. Marubbio:

We thought of that but the levels were so much higher than what people report in intestinal conditions that we suspected that it was due to pancreatic damage.

Dr. ten Bensel:

Is there any evidence that desferoxamine gives a high amylase level? I really can't comment. Does anyone have any information about a high amylase level in iron toxicity?

This was a very high dose of iron and, if the serum iron value is above 500 mcg.%, one should obtain baseline studies for coagulation and liver function and electrolytes. The literature is not 100% in agreement on just how one should proceed at this point.

I have had experience with desferoxamine, exchange transfusions, and peritoneal dialysis in children. Renal dialysis does not remove cellular iron. Iron goes very rapidly into the cytoplasm and most authors feel that the kelating agents are the best. Experimental data in dogs using both exchange transfusion and desferoxamine; exchange transfusion is the most efficient procedure.[1] I have been involved in half a dozen cases in children with immediate exchange transfusion in an attempt to remove the iron. A child can be exchanged easier than an adult because of his smaller transfusion requirements. A two and one-half volume exchange transfusion is the criteria used. Desferoxamine given orally hasn't been proven effective. I still use it since it has no demonstrated harmful side effects. When one has a level of serum iron over 500 mcg./M, you would start by giving 90 mg./Kg. of desferoxamine in a 5% solution intravenously. Then titrate your therapy on the basis of your serum iron level. The dose of desferoxamine is given intravenously over an hour. It shouldn't be given in a single bolus as there have been some adverse reactions.

Peritoneal dialysis has also been shown to be an effective way of removing kelated iron. Peritoneal dialysis is also relatively easy to perform.

Dr. John Crosson:

Do you think a plasmaphoresis would be as effective as an exchange transfusion?

Dr. ten Bensel:

With free iron in the plasma, I imagine it probably would be as effective. It might be worth a try.

Dr. John Tobin:

I was wondering why her anuric stage was felt to be contraindication to the use of desferoxamine? It seems to me if it's possible to kelate the iron, it makes little difference if it is kelated in the circulation or if it is being excreted in the urine.

Dr. ten Bensel:

I think the literature states that you should not use desferoxamine in renal failure.

Dr. Schiller:

The desferoxamine has to be cleared through the kidneys since it is the only route that is available to it. There is some suggestion that renal dialysis may be helpful. There is the possibility in this case that it could have been used but desferoxamine itself is a rather potent toxic agent if it is not cleared, so in people who have anuria, even though you have the kelated iron there, they show no improvement. It is not very clear by the way how desferoxamine really does its thing.

Dr. Seeds:

I just wanted to ask about the fetal organs. Were there any studies done on the fetus? I think anytime the mother gets that kind of a level, you have to think that a similar level is affecting the fetus.

Dr. ten Bensel:

Iron stains done on the fetal organs and placenta were negative.

Another physician: If I can relate a case I was involved in in the spring of 1973 at this hospital, it would underscore your statement about early treatment and also to emphasize that iron ingestion is not innocuous. We had a 17 year old who was seen in the emergency room after ingestion of an unknown amount of iron. The interns in the emergency room recognized that this was an emergency situation and the ward team was called down and he was given Ipecac and vomited. No pills came out but a flat plate showed a bezoar of perhaps 10 or 12 cm. in size of iron. A large bore tube was passed and he was lavaged with sodium bicarbonate and given oral desferoxamine. We admitted him to the ward and followed his tablets through the G.I. tract, continually giving him oral desferoxamine, bicarbonate and maalox. He passed 40 or 50 tablets in his stool that were still legible and you could read the drug inscription. His serum iron went to 450 mcg.% and he was treated without parenteral desferoxamine. They were ferrous sulfate tablets his girlfriend got from the OB-GYN Department.

Dr. ten Bensel:

I checked with the pharmacy and there is only one type of ferrous sulfate tablet given out by the pharmacy. Let me just say a word about primary prevention. There are 2,000-3,000 cases a year of iron poisoning. The last study I saw put iron as the fourth most common ingestion in children and the PDR lists approximately 120 dosage forms of iron. Significant amounts of iron are given to the obstetrical population. The recommendation is if there are children in the house, one should not give more than a one month supply at one time.

Dr. Kenneth A. Osterberg:

I have a question of where the physician stands in a medical-legal instance if desferoxamine is given since the package insert warns about skeletal abnormalities and the warning not to give it during pregnancy and you go ahead and give it, and the child is born with congenital abnormalities? Where does that doctor stand in the law court?

Dr. ten Bensel:

I guess that would have to be answered at that point. I would certainly have given the oral desferoxamine early without any worry because if it is not absorbed, I feel Dr. Seeds made a good point that the mother's life would come before the baby's. That is a risk one has to take and what happens to the fetus would have to be determined at a later time. There aren't too many cases where this has happened and I wouldn't be too concerned about the legal implications of the problem.

Dr. Schiller:

I would like to state that there were two more cases here in the spring of 1973, both of which received desferoxamine and another case was seen at Lutheran Deaconess Hospital. All of these people have survived ingestion of various amounts, between 40 and 100 tablets, and as far as we know all the infants are normal. These patients were treated with either intravenous or intramuscular desferoxamine so in spite of this unfortunate case, people in the community are now more aware of the problem.

Reference

1. Whitten Charles F et al.: Studies in acute iron poisoning. Pediatrics 38:102, July 1966.

Testing in Humans: Who, Where & When.

the weight of ethical opinion:

Few would disagree that the effectiveness and safety of any therapeutic agent or device must be determined through clinical research.

But now the *practice* of clinical research is under appraisal by Congress, the press and the general public. Who shall administer it? On whom are the products to be tested? Under what circumstances? And how shall results be evaluated and utilized?

The Pharmaceutical Manufacturers Association represents firms that are significantly engaged in the discovery and development of new medicines, medical devices and diagnostic products. Clinical research is essential to their efforts. Consequently, PMA formulated positions which it submitted on July 11, 1975, to the Subcommittee on Health of the Senate Labor and Public Welfare Committee, as its official policy recommendations. Here are the essentials of PMA's current thinking in this vital area.

1. PMA supports the mandate and mission of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and offers to establish a special committee composed of experts of appropriate disciplines familiar with the industry's research methodology to volunteer its service to the Commission.

2. PMA supports the formation of an independent, expert, broadly based and representative panel to assess the current state of drug innovation and the impact upon it of existing laws, regulations and procedures.

3. When FDA proposes regulations, it should prepare and publish in the *Federal Register* a detailed statement assessing the impact of those regulations on drug and device innovation.

4. PMA proposes that an appropriately qualified medical organization be encouraged to undertake a comprehensive study of the optimum roles and responsibilities of the sponsor and physician when company-sponsored clinical research is performed by independent clinical investigators.

5. PMA recognizes that the physician-investigator has, and should have, the ultimate responsibility for deciding the substance and form of the informed consent to be obtained. However, PMA recommends that the sponsor of the experiment aid the investigator in discharging this important responsibility by providing (1) a document detailing the investigator's responsibilities under FDA regulations with regard to patient consent, and (2) a written description of the relevant facts about the investigational item to be studied, in comprehensible lay language.

6. In the case of children, the sponsor must require that informed consent be obtained from a legally appropriate representative of the participant. Voluntary consent of an older child, who may be capable of understanding, in addition to that of a parent, guardian or other legally responsible person, is advisable. Safety of the drug or device shall have been assessed in adult populations prior to use in children.

7. PMA endorses the general principle that, in the case of the mentally infirm, consent should be sought from both an understanding subject and from a parent or guardian, or in their absence, another legally responsible person.

8. Pharmaceutical manufacturers sponsoring investigations in prisons must take all reasonable care to assure that the facilities and personnel used in the conduct of the investigations are suitable for the protection of participants, and for the avoidance of coercion, with a respect for basic humanitarian principles.

9. Sponsors intending to conduct nontherapeutic clinical trials through the participation of employee volunteers should expand the membership and scope of its existing Medical Research Committee, or establish such an internal Medical Research Committee, with responsibility to approve the consent forms of all volunteers, designs, protocols and the scope of the trial. The Committee should also bear responsibility to ensure full compliance with all procedures intended to protect employee volunteers' rights.

10. Where the sponsor obtains medical information or data on individuals, it shall be accorded the same confidential status as provided in codes of ethics governing health care professionals.

11. PMA and its member firms accept responsibility to aid and encourage appropriate follow-up of human subjects who have received investigational products that cause latent toxicity in animals or, during their use in clinical investigation, are found to cause unexpected and serious adverse effects.

12. PMA supports the exploration and development by its member companies of more systematic surveillance procedures for newly marketed products.

13. When a pharmaceutical manufacturer concludes, on the basis of early clinical trials of a basic new agent, that a new drug application is likely to be submitted, a proposed development plan accompanied by a summary of existing data, would be submitted to the FDA. Following a review of this submission, the FDA, and its Advisory Committee where appropriate, would meet with the sponsor to discuss the development plan. No *formal* FDA approval should be required at this stage. Rather, the emphasis should be on identification of potential problems and questions for the sponsor's further study and resolution as the program develops.

The PMA believes that health professionals as well as the public at large should be made aware of these 13 points in its Policy on Clinical Research. For these recommendations envisage constructive, cooperative action by industry, research institutions, the health professions and government to encourage creative and workable responses to issues involved in the clinical investigation of new products.

P·M·A

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MSMA Highlights

Division of Socio-Economic Affairs

A LITTLE OVER one year ago the House of Delegates of the Minnesota State Medical Association increased the Association's dues by $100. One-half of that increase was ear-marked by the House to strengthen and increase the Association's programs related to the socio-economics of medicine.

As a result, the Division of Socio-Economic Affairs, a newly established entity within the committee and staff structure of the Minnesota State Medical Association, is now a reality.

In establishing this new Division, the House recognized the increasing impact socio-economic forces have on the practicing physician in Minnesota. This fact is best illustrated by looking at some of the challenges faced by the new Division of Socio-Economic Affairs.

Relationship with Government

First, the Division represents the Association in relationships with the Minnesota State Legislature. Here the Division presents the Association position on health bills under consideration by the House of Representatives and the Senate.

Influencing legislation is not the full extent of involvement with state government. The Division also must maintain daily working relationships with state agencies and regulatory bodies. Included are relationships with the Department of Public Welfare, State Health Department, Medical Examining Board, other certification and licensure boards of the allied health professions, the State Health Coordinating Council which is part of the health planning legislation, Insurance Commissioner's office on matters dealing with health and professional liability insurance, and a number of other bodies within the executive branch of Minnesota government.

While the Division's primary attention is focused on state government, actions of the federal government which have a direct effect on Minnesota must be monitored by the Division of Socio-Economic Affairs with the assistance of the American Medical Association. Another function of the Division is the working relationship with the Foundation for Health Care Evaluation, Blue Cross/Blue Shield, PSROs and health maintenance organizations. The passage of Public Law 93-641, the National Health Planning and Resources Development Act of 1974, opens a whole new area of concerns to be faced by the Minnesota State Medical Association. In this program and in others, the Division will act to coordinate the effort of physicians to help them relate more effectively to the socio-economic process.

MINNPAC remains a high priority as its effectiveness has an overall strengthening effect on the socio-economic goals of the Association.

The challenges facing this Division are many. As can be seen by the foregoing, to meet them, a whole new committee structure has been created to bring together the existing socio-economic programs of the Associaton with the new potential problems represented in the health planning legislation.

New Legislative Committee

A new Legislative Committee will be established to assume the role of the now dissolved Public Policy Committee. The Legislative Committee, however, will have some additional responsibility. Where the Public Policy Committee was limited to generating physician support for medicine's position on health legislation, the new Legislative Committee will help establish those Association positions. Health legislation will be reviewed by the Committee and recommendations for support or non-support will be made. In addition, proposed health legislation will be drafted by the Legislative Committee when appropriate, for introduction to the legislature by the Association. Throughout this process, the Committee will receive substantial input such as bill summaries and analyses from the staff of the Division.

Health Planning Committee

The second committee under this new structure represents a new function of the state Association. This is the Health Planning Committee, responsible for developing guidelines to facilitate physician involvement in the health planning process generated by congressional enactment of Public Law 93-641.

Passage of this federal legislation has raised significant questions for physician members of the Minnesota State Medical Association. Some of them include:

How should physicians contribute to health planning as members of HSA's . . . Health Systems Agency Boards?

How should physician advisory committees function in relationship to the seven HSA Boards in Minnesota?

What role, if any, should your state Association take in working with other health provider organizations in the state as they seek to develop a coordinated approach to help guide actions of the consumer-dominated HSA Boards?

What policies will we as an Association formulate and send to the state health planning bodies concerning such vital health planning issues as Certificate of Need?

How much physician representation should we demand in the health planning process?

These questions and others will be the concern of the Association's new Health Planning Committee.

Medical Service Committee

The third committee within the Division of Socio-Economic Affairs is the Medical Service Committee. The Committee's function will remain the same—addressing such vital issues as third-party reimbursement and relationships with organizations such as Blue Cross/Blue Shield, PSROs, HMOs, Foundations and others related to the practice of medicine.

These three Committees—Legislative, Health Planning, and Medical Service—will report through their chairmen to a new Socio-Economic Board whose members are the same as the Executive Committee of the Council. The combined mechanism of the Socio-Economic Board and the Executive Committee will permit immediate policy action on recommendations made by any one of the Committees in those instances when time is of the essence. This need for fast action, sometimes by telephone conference, is absolutely vital due to the rapid developments during a session of the state legislature and in other activities of state government.

The Division of Socio-Economic Affairs, as is true with all activity of the Association, will be effective through the combined efforts of physician members and the daily activity of staff.

Management Team

Coordinating the effort is a management team headed by the Director of the Division, Mr. James W. Rosevear. Mr. Rosevear comes to the staff of the Minnesota State Medical Assoication after serving eleven years on the staff of the American Medical Association. As Division Director, he reports to the Association's Executive Vice President, Mr. Harold W. Brunn.

The Division has three departments. The Department of Governmental Affairs is directed by Mr. James H. Sova who will staff the new Legislative Committee, continue as chief lobbyist for the Association and provide staff assistance to the MINNPAC Board of Directors. Assisting in this Department is Mr. Rick Teske who reports directly to the Division Director on a variety of assignments designed to provide better communication between the state Association and its physician members. In addition, Mr. Teske will provide backup assistance to Mr. Sova during sessions of the state legislature.

Mr. Tom Galligan is Director of the new Department of Health Planning. Mr. Galligan comes to the Association staff having served on the staff of the Foundation for Health Care Evaluation and will staff the new MSMA Health Planning Committee. In addition to these duties, Mr. Galligan will work in each of the seven health service areas to assist physicians in their relationship to the health planning process.

Ms. Lois Wilzewske will direct the third Department—the Department of Socio-Economic Research. One of her responsibilities will be to staff the Medical Service Committee. A major portion of her time will be devoted to the preparation of research documents, summaries and analyses for use by other members of the Division staff and its three committees. This effort will be crucial to the response the Association ultimately makes on legislative and health planning issues.

Assistant to the Director and coordinator of secretarial services for the Division is Mrs. Ann Scholle.

This Division staff is dedicated to bringing new programs into being in response to the needs of the Association as physician members relate to the increasing challenges represented by the socio-economics of medicine. Better communication with physicians throughout the state of Minnesota is a key priority and each Division staff member along with the Association leadership will be seeking opportunities to meet with county medical societies during the coming year. The objective is ambitious—to cover as many county societies as possible. A special letter over the signature of Association President, Richard E. Anonsen, M.D. will be directed to the presidents of all county societies seeking an opportunity during the balance of 1976 and 1977 to discuss the significance of socio-economic programs before their membership.

The Division will publish a new socio-economic newsletter which will be distributed to physicians and others directly involved in socio-economic programs of medicine within the state of Minnesota. In addition, the Division has accepted the invitation of MINNESOTA MEDICINE to prepare this page in each issue as a means of updating physicians on socio-economic topics of current interest.

Summary

This is what one-half of the MSMA dues increase is providing. But a dues increase, new committee structures, expanded staff capability and other initiatives will be ineffective without the continued support and involvement of individual physicians throughout the state of Minnesota. The ultimate influence of the Association's action on socio-economic concerns can only be felt when its members make their wishes known and power felt. It is the job of the new Division of Socio-Economic Affairs to help physicians coordinate this effort and thereby create a strong socio-economic force for the Minnesota State Medical Association.

Annual Meeting

Annual Bleating . . . Not all Baa-d.

"The cry of a sheep ; to talk complainingly . . ." That's how Webster's Dictionary defines the word "bleat." Daniel Webster didn't attend CME '76 in Rochester. For those who did, a more appropriate definition might read:

> *"Bleat (V., in medicine to gripe): Angry mouthings relating to tired feet, loss of registration booth, being in one hotel when you should be in the other . . ."*

While bleatings dealt with physical liabilities of the meeting site, the many positive remarks were related to the fine scientific program content, excellent staffing, and the array of well planned social activities. Whether complaining or complimenting, attendees of CME '76 were right.

A complete evaluation of the Annual Meeting will follow. For now, I'd like to thank all who attended the Meeting and special thanks to the many who aided in the production of it. Oh, and thanks too, to those whose vote of confidence we earned. It was pleasing to hear that CME '76 wasn't all bad. Actually, you said it "wasn't bad at all." And, that made many of us feel really good.

R. D. Semsch, M.D.
Chairman
Scientific Assembly

Obesity Seminar

Minnesota Seminars in conjunction with the Minnesota State Medical Association will present a seminar on "Obesity" on January 13 to January 19 in Tobago, West Indies. Details will follow in the next issue.

Perinatal Mortality

The Changing Patterns of Perinatal Mortality at a Suburban Community Hospital

SYLVESTER J. SANFILIPPO, M.D.*

This report describes the total perinatal mortality experience of a suburban community hospital from its beginning in October 1965 through 1974. The obstetrical patients were educated, middle-class, white and predominately of northern European ancestry. The hospital's neonatal mortality rates were generally lower than the Minnesota and white USA rates from 1966-1974. Perinatal mortality rates and fetal death rates of the hospital were likewise generally lower than the Minnesota rates. A moderate reduction of the hospital's perinatal mortality was noted during the 1973-1974 period and coincided with the increased application of advances in perinatology and with more efficient use of regional neonatal intensive care units. The neonatal mortality rate, fetal death rate and perinatal mortality rate of the hospital's 1973-1974 cohort were 22% less, 31% less and 25% less respectively than the corresponding perinatal rate of the hospital's 1966-1974 cohort.

THIS REPORT IS a preliminary outline of the neonatal, fetal and perinatal mortality experience at Fairview-Southdale Hospital (FSDH)[†], a private community hospital situated in Edina, a middle-class suburb of Minneapolis, Minnesota. Since 1968 more live births have been delivered annually at FSDH than at any other hospital in the state. These newborns have comprised 4.5 to 5% of the state's total number of live births each year.

Definitions

A specific term such as "live birth" may impart different meanings for individuals in other institutions, regions, states or nations. A glossary of terms is included in order to define precisely the data.

Live Birth—any completely delivered newborn displaying a heart beat, respiratory effort or any sign of life regardless of gestational age or weight, unless otherwise indicated, eg, live births weighing over 500 grams.

Fetal Death (Stillbirth)—death of a fetus (20 weeks or more of gestation) prior to complete delivery from the mother.

Neonatal Death—death of a live birth during the first 28 days of life.

Neonatal Mortality Rate—number of neonatal deaths per 1000 live births. Neonatal mortality rate with a specific upper or lower weight limit signifies the number of neonatal deaths with a specific upper or lower weight limit per 1000 live births having the same specified weight limit.

Fetal Death Rate or Ratio—number of fetal deaths per 1000 live births.

Perinatal Mortality Rate or Ratio—sum of the fetal deaths and the neonatal deaths per 1000 live births.

Birth Cohort—number of live births or fetal deaths in a specific year or series of years. Each neonatal death is assigned to its original birth cohort.

Materials and Methods

Patients

During the total study period commencing with October, 1965 and ending December 31, 1974, there were 24,832 deliveries producing live births. Out-of-wedlock mothers accounted for 2% of the deliveries. More than 98% of married mothers and more than 98% of the out-of-wedlock mothers were white. The three principle lines of genetic heritage were Norwegian, Swedish and German.

No live births or fetal deaths were excluded from the study. Among the live births were 243 sets of twins and three sets of triplets.

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*Pediatrician in private practice with Schaffhausen & Sanfilippo, Chartered, Minneapolis, Minnesota, and member of the Pediatric Task Force of the Health Board of the Metropolitan Council, St. Paul, Minnesota. Member of the Fairview-Southdale Hospital Medical Staff, Edina, Mn. Associate member of the University of Minnesota Hospitals Medical Staff, Minneapolis, Minnesota.

[†] FSDH is a non-profit, acute and general care hospital located in Edina, Mn. The facility was newly constructed and opened for service in October, 1965.

Personnel

Nursing care was provided by the hospital nursing staff. Nurses specialized in delivery room care, postpartum care or newborn nursery care and nursing staff assistants augmented the postpartum and newborn nursery care.

The private physicians of the hospital medical staff supplied the obstetrical and medical care. By 1974, roughly 40 family physicians, 36 obstetricians and 33 pediatricians were actively engaged in this role. Obstetricians performed about 80% of all deliveries. Two pediatric groups utlized pediatric nurse practitioners in the newborn nursery.

Facilities

Fetal monitoring has been practiced at FSDH since 1973. A transitional care nursery for the observation and care of newborns during the period immediately after birth and an intermediate care nursery for the care of prematures and sick newborns has existed since the origin of the hospital. In 1973, nurses specially trained in the care of moderately and severely ill newborns and skilled in the use of cardio-respiratory monitoring devices, assumed charge of the newborn nurseries. The first transfer of a high-risk newborn to a regional neonatal intensive care unit occurred in 1968 and by 1974 virtually all high-risk infants were transported to a neonatal intensive care center.

Data for Study

Data for this study were obtained from infant and maternal hospital charts, delivery room ledgers, nursery ledgers and record room reports. The perinatal vital statistics of Minnesota residents were sent to us by Harriet J. Kelly, Ph.D., Linda K. Nelson and Linda J. Lennes, Section of Health Statistics, Minnesota Department of Health. The cross-matching of the birth and death certificates of all infants born at FSDH enabled us to account for not only the neonatal deaths at FSDH, but also those happening elsewhere. A listing of FSDH fetal deaths by the Section of Health Statistics helped in correcting errors of omission. The cross-examination of data from multiple sources was necessary to ensure complete and accurate information.

Results

The important events in the analysis of perinatal mortality statistics are the number of live births, neonatal deaths, fetal deaths and the peri-

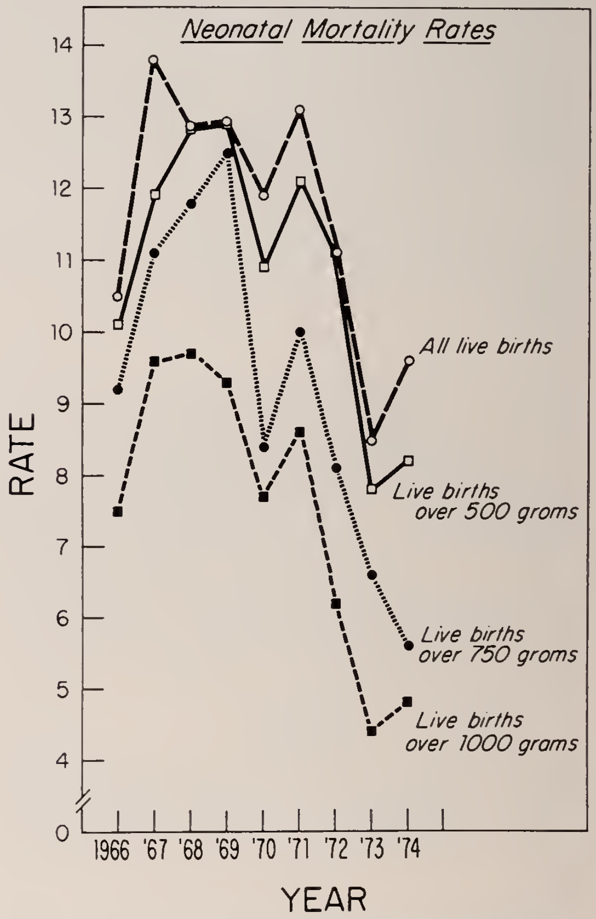

Fig. 1—FSDH neonatal mortality rates according to weight.

TABLE I
FSDH Perinatal Statistics

Event	Birth Cohorts										
	*1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1966-1974	1965-1974
Live Births	325	2278	2617	2896	3027	3116	2818	2605	2709	2696	24,762	25,087
Neonatal Deaths	1	24	36	37	39	37	37	29	23	26	288	289
Fetal Deaths	5	28	27	20	28	23	31	27	16	17	217	222
Neonatal Mortality Rate	—	10.5	13.8	12.8	12.9	11.9	13.1	11.1	8.5	9.6	11.6	11.5
Fetal Death Rate	—	12.3	10.3	6.9	9.2	7.4	11.0	10.4	5.9	6.3	8.8	8.8
Perinatal Mortality Rate	—	22.8	24.1	19.7	22.1	19.3	24.1	21.5	14.4	15.9	20.4	20.4

*Oct., Nov. and Dec., 1965

natal rates derived from these figures (Table 1). The findings are expressed in terms of individual annual birth cohorts from 1965 through 1974, a nine-year birth cohort from 1966-1974 and a nine-year and three-month birth cohort from October 1965-1974. Since events in the 1965 cohort did not cover an entire year, perinatal rates were not calculated for 1965.

Variability is inherent in plotting annual fetal death rates and neonatal and perinatal mortality rates of the small population of FSDH patients. Consequently the definitive trend of each rate is partially obscured (Figures 1, 2 and 3). To compensate for this problem, the recent 1973-1974 cohort value of a specific perinatal rate is compared with the same rate for the 1966-1974 cohort (Table 2). Similarly the recent average of the 1973 and 1974 values of a perinatal rate is compared with the average value of the rate during 1966-1974 in considering the state and national results. Except for insignificant differences in the 1966-1974 fetal death rate and the 1973-1974 neonatal mortality rate, each multiple-year FSDH perinatal rate, whether calculated as a cohort rate or an average rate, was identical.

The disproportionately low number of neonatal deaths in 1965 and the low neonatal mortality rate in 1966 (Table 1, Figures 1 and 2) were likely due to the untested capability of the new obstetrical and nursery services. This created a tendency to deliver high-risk mothers to more

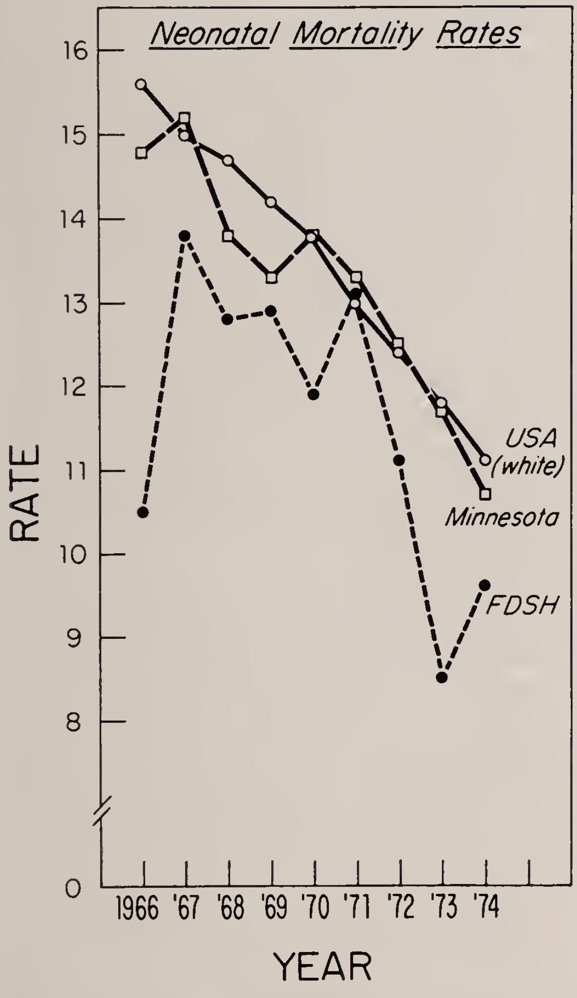

Fig. 2—Neonatal Mortality Rates: a comparison of FSDH, Minnesota and white USA results. The 1974 USA rate is provisional.

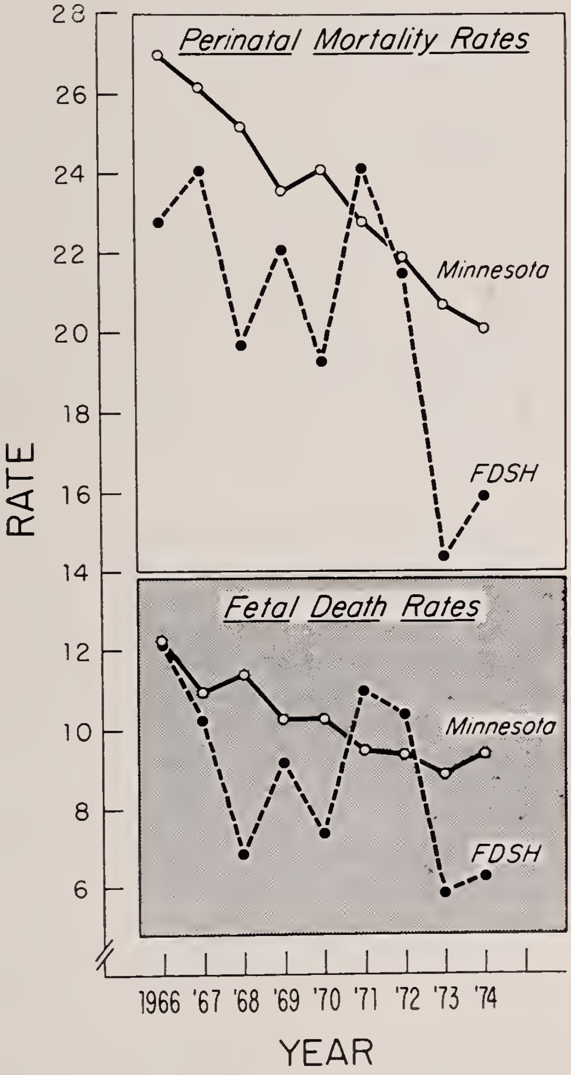

Fig. 3—Perinatal Mortality Rates and Fetal Death Rates: a comparison of FSDH and Minnesota results.

established hospitals in the area. Furthermore, there were no live births weighing 1000 grams or less in 1965 and only eight live births in that weight category were born in 1966 compared with an average of 12 per year from 1967-1974. These facts favored a low neonatal mortality rate considering that neonates weighing 1000 grams or less had a neonatal mortality of 97% in the 1966-1974 cohort. Chase[1] reported a neonatal mortality rate of 924.1 (92% mortality) for white newborns weighing 1000 grams or less in a 1960 matched U.S. birth cohort study. Mortality of infants weighing less than 1000 grams and treated in an intensive care nursery was 87% in one study[2] and 84% in another.[3]

A moderate decline in all three FSDH perinatal rates took place in 1973 and 1974 (Tables 1 and 2; Figures 1, 2 and 3). The neonatal mortality rate, fetal death rate and perinatal mortality rate of the 1973-1974 cohort were 22% less, 31% less and 25% less respectively than the corresponding perinatal rate of the 1966-1974 cohort (Table 2).

TABLE 2
Reduction of Perinatal Mortality Statistics in 1973-1974

Rates	1966-1974	1973-1974	% Change
Neonatal Mortality Rate			
FSDH	11.6	9.1	−22
Minnesota	13.2	11.2	−15
USA (White)	13.5	11.4	−16
Fetal Death Rate			
FSDH	8.8	6.1	−31
Minnesota	10.3	9.2	−11
Perinatal Mortality Rate			
FSDH	20.4	15.2	−25
Minnesota	23.5	20.4	−13

The uppermost curve in Figure 1 depicts the trend of annual neonatal mortality rates for all live births regardless of weight. This includes non-viable births (500 grams or less), borderline viable births (501-1000 grams) and viable births (over 1000 grams). The second uppermost curve excludes the non-viable live births and thereby obtains improved neonatal mortality rates except for 1968, 1969 and 1972 when there were no live births of 500 grams or less. The curve for live births over 750 grams eliminates not only the non-viable live births, but also the borderline viable prematures with the least chance of survival (501-750 grams). The result is a tracing with even lower neonatal mortality rates. The lowest curve representing viable neonates over 1000 grams yields the best neonatal mortality outcome and clearly demonstrates the advantage of anatomic and physiological maturation in determining neonatal survival. Only 0.42% of the 1966-1974 cohort weighed 1000 grams or less, but those births were responsible for 35% of all deaths in the cohort.

All four weight groups showed a substantial decline in neonatal mortality after 1971. The neonatal mortality rate for live births weighing over 1000 grams was 4.4 in 1973 and 4.8 in 1974 with a percent mortality of 0.44% and 0.48% respectively. The latter values fall within the "white zone" of mortality less than 0.5% reserved for low-risk newborn infants at term.[4]

Figure 2 compares the pattern of neonatal mortality rates for FSDH, the state of Minnesota[5] and the white live births of the United States[6] during the 1966-1974 time span. The FSDH neonatal mortality rates were lower than the Minnesota and white USA rates, except in 1971 when the FSDH neonatal mortality rate slightly exceeded the national figure. FSDH exhibited the greatest reduction in neonatal mortality after 1971. The Minnesota and white USA 1973 and 1974 average neonatal mortality rates each dropped 15-16% below its corresponding 1966-1974 average rate (Table 2).

A Minnesota single birth cohort study (1967-1970) noted a total neonatal mortality rate of 14.0 and a white neonatal mortality rate of 12.5.[7] The FSDH birth cohort for 1967-1970 had a neonatal mortality rate of 12.8. Minnesota resident births during 1970-1973 were 4.3% non-white,[7] while the FSDH births were less than 2% non-white.

The perinatal mortality rates and fetal death rates of FSDH and the state of Minnesota are illustrated in Figure 3. Except for 1971, lower perinatal mortality rates prevailed at FSDH during the nine-year period. The FSDH perinatal mortality rate of the 1973-1974 cohort was 25% less than the rate of its 1966-1974 cohort while the Minnesota average perinatal mortality rate for 1973-1974 was 13% less than its average rate for 1966-1974 (Table 2).

The fetal death rate at FSDH was less than the Minnesota fetal death rate in six of the nine years from 1966-1974 (Figure 3). The FSDH fetal death rate of the 1973-1974 cohort was 31% below the 1966-1974 cohort rate. Minnesota's average fetal death rate for 1973 and 1974 was 11% under the state's average rate for 1966-1974 (Table 2).

Discussion

Perinatal medicine strives to reduce perinatal mortality to its irreducible limit. After an extensive analysis of perinatal deaths among 13,378 births weighing over 1000 grams, Usher proposed irreducible minimums for perinatal, stillbirth (fetal death) and neonatal mortality rates.[8] The irreducible lower limits were estimated as 9.0 for the perinatal mortality rate, 6.4 for the stillbirth rate and 2.6 for the neonatal mortality rate.

The disappointing perinatal mortality statistics for FSDH in 1971 prompted a survey of perinatal mortality from 1965 to 1971.[9] Considering the hospital's well-trained and conscientious staffs, modern facilities and educated middle-class patients, the results were less than impressive. The findings were shared with the FSDH medical staff and engendered an awareness of the perinatal mortality problem. A decline in perinatal mortality occurred after 1971 and was most marked in modern facilities and educated, middle-class pa- 1973 and 1974. The stillbirth (fetal death) rate of 4.4 per 1000 births weighing over 1000 grams at FSDH in 1973 constituted a reduction of the "irreducible" minimum stillbirth rate of 6.4.

Conclusions

The present study uncovered no single cause to explain the improved perinatal results of the 1973-1974 cohort. Several conditions, however, coexisted with the period of improvement. The wealth of physiological and technical knowledge in the field of perinatology was being increasingly applied to clinical obstetrics and neonatology. The help of nurses with specialized training in neonatal intensive care and the early transfer of nearly all high-risk newborns to regional intensive care units were additional special features of the 1973-1974 era at FSDH.

Abortion was legally sanctioned in 1973, thus introducing another variable. Its influence was probably minor compared with the previously mentioned coexisting conditions. However, there are insufficient data to assess the relative significance of legalized abortion as a factor responsible for the reduction of perinatal mortality at FSDH during the 1973-1974 period.

Closing Comments

Optimism in the continuing reduction of perinatal mortality is justified by results accruing from the rapid advances in perinatology and the regionalization of perinatal care. During the past decade the science of perinatology has grown and differentiated from an embryonic activity to a mature and productive discipline represented in the subspecialties of maternal and fetal medicine and neonatology. Within the past eight years planned regionalization of perinatal care has proved to be an effective means of decreasing perinatal mortality.[10,11] Simultaneously, many community hospitals throughout the nation have developed impromptu regionalization of neonatal care by informally establishing networks of referral and consultation with regional neonatal intensive care units. The FSDH experience reported in this paper provides results obtained in an informal regional neonatal care system. The need for well-planned regionalization of perinatal care nonetheless exists.

Guidelines for development of regional perinatal care in Minnesota are currently being prepared. They will be an adapted version of guidelines formulated by the Committee on Perinatal Health and recently published in condensed form.[12]

I agree with Nesbitt[13] who states that ". . . we need much more basic information about the true status of obstetrics and newborn care in this country before we can remedy deficiencies and establish a more effective program."

Summary

The patient profile, the professional services profile and the profile of perinatal mortality statistics of FSDH from October 1965 through December 1974 are described. Prior to 1973 the perinatal mortality statistics profile, a performance indicator, was mediocre in relation to the advantaged patient and professional services profiles. An encouraging reduction in perinatal mortality was noted in the 1973-1974 period. The improved perinatal rates evolved within the context of better maternal-fetal management practices, the use of nurses skilled in neonatal intensive care, and the more efficient utilization of regional neonatal intensive care units.

The FSDH neonatal mortality rates were compared with the Minnesota and white USA neonatal mortality rates over a nine-year period (1966-1974). Similarly, the FSDH perinatal mortality rates and fetal death rates were compared with Minnesota's perinatal mortality rates and fetal death rates from 1966-1974. The FSDH perinatal rates were generally lower than both the state and national rates and displayed a greater decline in the 1973-1974 period. The neonatal mortality rate, fetal death rate and perinatal mortality rate of the FSDH 1973-1974 cohort were 22% less, 31% less and 25% less respectively than the corresponding perinatal rate of the FSDH 1966-1974 cohort.

Acknowledgments

Co-workers in this project were record room staff members, delivery room nurses, newborn nursery nurses and my daughter. They contributed greatly in data collection and data verification. The assistance of the Section of Health Statistics, Minnesota Department of Health was crucial to the accuracy and breadth of the study. The help of all these persons is greatly appreciated.

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Letters to the Editor

We would like to encourage physicians to contribute to the Letters to the Editor Section. We want to hear what you have to say, what you think, why you hold certain opinions. In short, we want to make this as lively and spirited a section as possible.

The Editors

Southern Minnesota Medical Association

The annual meeting of the Southern Minnesota Medical Association will be held September 25, in Albert Lea. The Kahler Motel is the meting place. Contact: Ethel A. McClane, Secretary, 1726 No. 4th St., Mankato 56001.

MSMA Launches Component Society Presentation Program

Component medical society presidents will be receiving a letter in the next few weeks from Minnesota State Medical Association President, Richard E. Anonsen, M.D. requesting an opportunity to present a special program during 1976 and 1977 on Association programs and membership benefits. The new Division of Socio-Economic Affairs will be highlighted by Association officers and staff through a slide-sound presentation first presented to the House of Delegates at the May, 1976 MSMA Annual Meeting in Rochester, Minnesota.

Book Reviews

HANDBOOK OF POISONING (Eighth Edition); Robert H. Dreisbach, M.D., Ph.D. Lange Medical Publications, Los Altos, California 1974. Price: $6.50.

This handbook is well compiled and excellently organized. It has a good index, in which any problem of poisoning can be readily identified and referred to. Most of the charts and chemical formulas serve an excellent purpose in giving the reader an opportunity to obtain a broader scope of the problem of poisoning.

It is surprising to read that the solanine tuberosum (potato green tuber, new sprout), and that shellfish harvested out of season could cause toxic reaction. Though one cuts away and discards the large leaf of the rhubarb, I had not anticipated that its oxalic acid content was sufficient to cause toxic effects.

Certainly this book should be immediately available for reference in all Emergency Centers, and should be of interest to any physician who is interested in the problem of poison.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus

HEAD NURSE by Barbara Villet (Doubleday and Company, Inc., Garden City, New York, 1975), 201 pages, $7.95.

This is one of the best medical novels I have ever read. It is an amazingly accurate portrait of the working day of an outstanding head nurse in a large, prestigious, underfunded and understaffed, teaching hospital.

The author did a painstaking job of research and each medical problem is accurately described in the language of a professional reporter. It is the best description I have ever seen of the dilemma of a three-year graduate who, despite her excellence, has no way to advance in her profession.

The flaws in the book are also readily apparent. Some of the descriptions of medical organizations are filled with cliches, but these are inserted as short asides and detract little from the emotional impact of the whole book. It should be required reading for nurses and doctors. I hope it sells a million copies.

John B. O'Leary, M.D.
Minneapolis, Minnesota

HANDBOOK OF PEDIATRICS. Henry K. Silver, M.D., C. Henry Kempe, M.D. and Henry B. Bryan, M.D. Tenth Edition. Lange Medical Publications, Los Altos, California, 1973. $6.50.

As a quick reference source the information in the handbook is quite acceptable. Topics covered are not too different from those in "Current Pediatric Diagnosis and Treatment" from the same publishers, and two of the same authors. More abbreviated format, greater number of tables, and lower price may win the house officer's vote for the handbook. At less than half the size of "Current Pediatrics," the handbook is still too bulky for comfortable carrying in a uniform pocket. Since the print used to gain compactness is small and difficult to read, I would choose the larger volume as a desk reference and look for a more convenient assemblage of frequently needed tables for pocket use.

Martha Strickland, M.D.
Uvalda, Texas

YOUR PROSTATE—Robert L. Rowan, M.D. and Paul Gillette, Ph.D. Doubleday & Company, Inc. 147 pages, $5.95.

This short book, written in elementary medical terminology, is designed to supply information for concerned patients afflicted with prostrate trouble or for others generally interested in the subject. Several chapters present aspects of anatomy, symptoms, diagnosis, and treatment which might be of some value for the nonmedical reader. These chapters include discussions of prostatitis, benign prostatic hypertrophy, and prostatic carcinoma.

The book contains errors which detract from its usefulness. Several examples could be listed, such as a statement that the gonococcus is the most frequent cause of prostatitis; symptoms of prostatism due to prostatic carcinoma appear at an early stage of the disease; partial prostatectomy is "radical" and that the treatment of benign prostatic hypertrophy is radical prostatectomy.

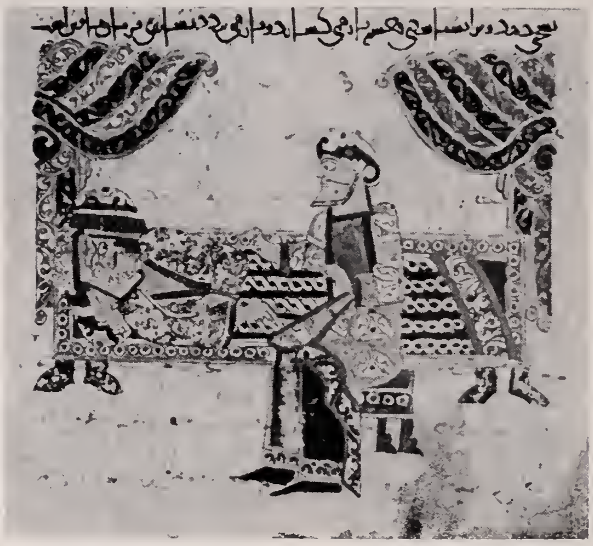
Conflicting statements occur. On page 40, the authors state that one-half of the patients with prostatic carcinoma are discovered while the tumor is confined to the prostate and that the five-year survival in this group is 55%. (Methods of treatment are not mentioned.) Later on page 105 the following appears: "rarely is the disease diagnosed early enough to be cured by destruction or removal of all cancer cells." Confusing statements regarding impotence, fertility, and retrograde ejaculation appear in a footnote on page 102.

Chapters are included dealing with premature ejaculation and the female prostate which do not seem germane to the subject at hand.

Although the book does have some merit, many urologists probably would not recommend it for reading by their patients.

W. E. Price, M.D.
Minneapolis, Minnesota

Bedside Medical Teaching Among the Arabs



Bedside medicine in eleventh-century Persia. The scribe who produced this illumination about 1090 A.D. paid no more heed to the rules of perspective than to the Muslim stricture against graphic representation of the human form. Courtesy Cincinnati Art Museum.

The hospital became the center of medical teaching at the Bimaristan in sixth-century Persia and among its lineal descendents, the medieval hospitals of the Arabs. Teachers then, as now, recognized the importance of actually seeing and examining patients as well as reading and attending lectures.

Medical education began early, usually at about age twelve or thirteen. Books were too rare and expensive for students to own; the formal lessons therefore consisted of the works of Hippocrates and the great Arab physicians read aloud to the students by a "Reading-out Physician," usually followed by a professor's discussion. The *Andarz Name* manuscript, dating from 1090 A.D. and from which the above illustration is taken, even included advice on bedside manner and personal grooming.

The most important part of the medical education was the clinical instruction in the hospital. The young student apprenticed himself to some senior practitioner, preferably one of wide and favorable reputation, and followed him round the wards in his daily visits, assisting in whatever way possible. More advanced or specialized studies could be arranged simply by transferring the apprenticeship to another physician. Rhazes was one of the most famous of the Arab bedside teachers; he is known to have set aside his most difficult cases for instructional purposes. Another widely-known medieval medical teacher, Abu al-Hakam, gathered all his students and staff physicians daily in the hospital library for discussions of interesting cases and of general medical problems.

Warren L. Kump, M.D.
Minneapolis, Minnesota

References

1. Elgood Cyril: A Medical History of Persia and the Eastern Caliphate. Cambridge University Press, 1951.
2. JAMA 213:1401. 1970.

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GENERALIST—Experienced generalist for multi-specialty medical center in north Twin Cities suburb. OB and Pediatrics optional. Liberal call schedule. Excellent fringe benefits, vacation and study leave. Box 80100, Saint Paul, Minnesota 55108.

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(Continued on page 504)

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(Continued from page 503)

EDINA—Opportunity for a family physician to join an established corporate group of seven physicians. Group currently consists of six family physicians and one general surgeon. Clinic is located approximately one quarter mile from a 450 bed hospital. Contact J. Turonie, Administrator at 612-920-5966.

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Index to Advertisers

Advertising Council 476
Allied Medical Audit Control, Inc. 506
Anderson, C. F., Co. 470
Burroughs-Wellcome Co. 459
Blue Shield/Blue Cross 466
Classified Advertising 503
Flint Laboratories 460, 461, 462
Health Care Systems 438
Kjell Bergh Borton Volvo, Inc. 436
Lilly, Eli & Co. 444, 476
London Realty, Inc. 476
Medical Protective Company 436
Pharmaceutical Mfrs. Assn. 490, 491
Roche Laboratories .... Cover 2, 435, 470, 471
Cover 3, Cover 4
Roerig and Company 474, 475
Smith, Kline & French 472
Volvo, Kjell Bergh's Borton 436
U.S. Navy Recruiting 442
Upjohn Company 473

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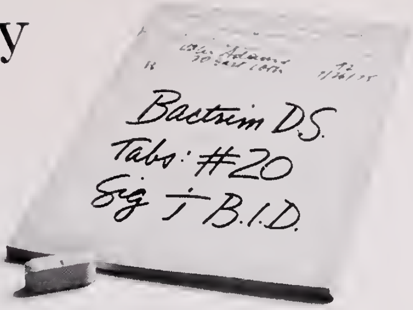
These conferences have been approved by the American Academy of Family Practice for Continuing Education and are held the second and fourth Thursdays from 8:30 to 9:30 a.m. in our Auditorium.

July 8, 1976	"Thyroid Carcinoma"	Fletcher Miller, M.D.
July 22, 1976	"Some Behavior and Gynecological Problems of Teenagers"	Elizabeth Jerome, M.D.
Aug. 12, 1976	"Pancreatitis"	William Brennom, M.D.
Aug. 26, 1976	"Malignant Hypertension"	Richard Gehrz, M.D. Charles Jarvis, M.D. Hugh Williams, M.D.

10-day Bactrim therapy outperforms 10-day ampicillin therapy.



In a multicenter, double-blind study of patients with chronic or frequently recurrent urinary tract infection, Bactrim 10-day therapy outperformed ampicillin 10-day therapy by 27.2%, when comparing patients who maintained clear cultures for eight weeks. Criterion for "clear culture" was 1000 or fewer organisms/ml of urine.

While adverse reactions noted in this study were mild (*e.g.*, vomiting, nausea, rash), more serious reactions can occur with these drugs. See manufacturer's product information for complete listing. Maintain adequate fluid intake; perform frequent CBC's and urinalyses with microscopic examination.

Note: Bactrim tablets were used in these clinical trials. Bioequivalency studies show one Bactrim DS double strength tablet is equivalent to two Bactrim tablets.

Bactrim™ DS

(160 mg trimethoprim and 800 mg sulfamethoxazole)

Double Strength tablets
Just 1 tablet B.I.D.

Bactrim™

(80 mg trimethoprim and 400 mg sulfamethoxazole)

2 tablets B.I.D.

For chronic or frequently recurrent cystitis and pyelonephritis due to susceptible organisms.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris* and *Proteus morganii.*

NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections. The recommended quantitative disc susceptibility method (*Federal Register, 37:*20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **Data are insufficient to recommend use in infants and children under 12.**

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) every 24 hours
Below 15	Use not recommended

Supplied: Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole — bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10.

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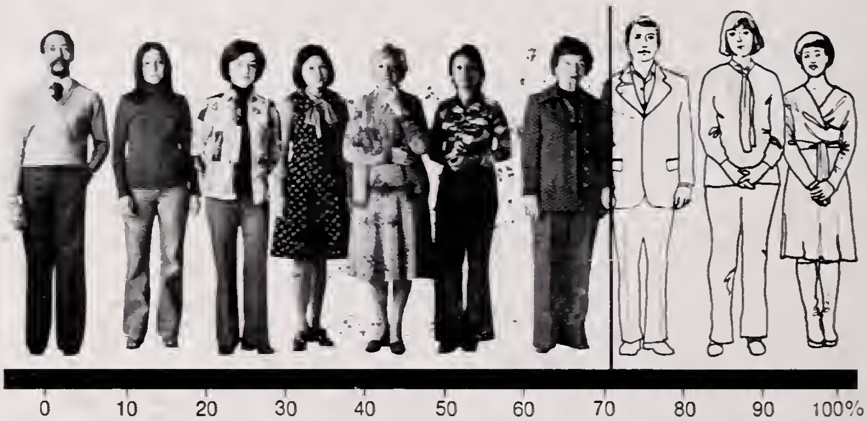
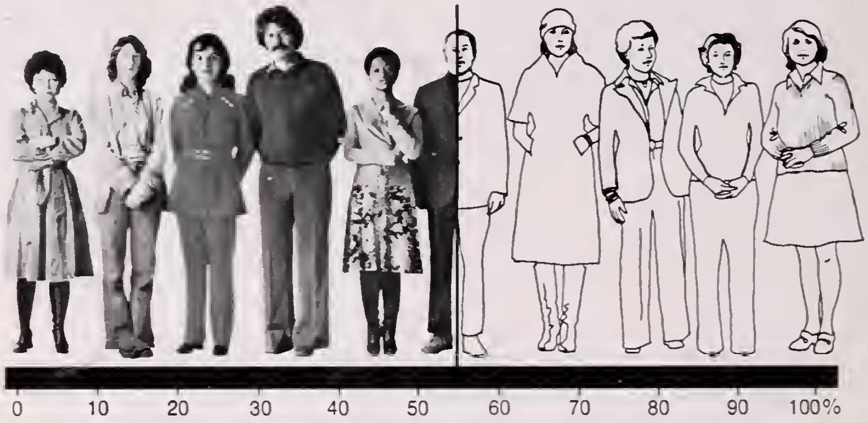


Bactrim–70.5% of 78 patients infection-free at 8 weeks.



ampicillin–55.4% of 74 patients infection-free at 8 weeks.

*This percentage is arrived at by the statistical method of dividing the difference between Bactrim and ampicillin results (15.1%) by the percent of ampicillin results (55.4%).

†Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

Bactrim™ DS

(160 mg trimethoprim and 800 mg sulfamethoxazole)

Double Strength tablets
Just 1 tablet B.I.D.

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Please see summary of product information on preceding page. ROCHE

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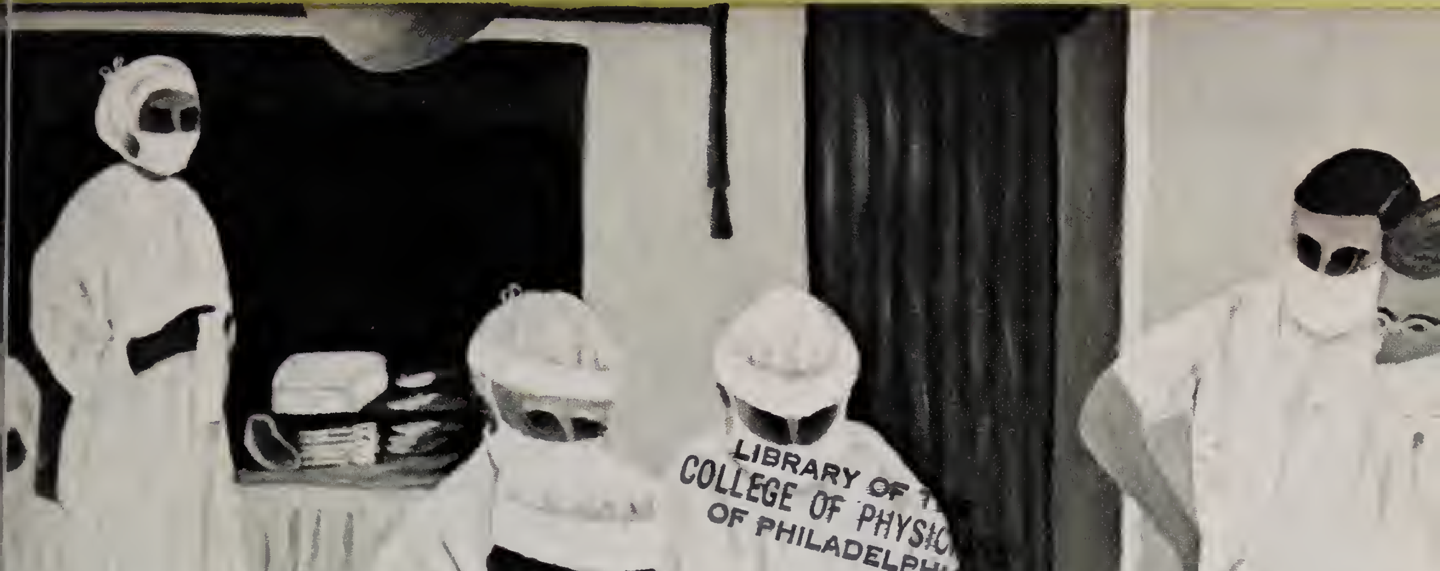

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AUGUST 1976

Both often

Predominant psychoneurotic anxiety
Associated depressive symptoms

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Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in freque
and/or severity of grand mal seizures n
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provide relief for both—as
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s associated with it are also
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id. This means that im-
vement is usually apparent
in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

Valium® (diazepam) Ⓘⓥ

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

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to habituation and dependence. In
gnancy, lactation or women of child-
ring age, weigh potential benefit
nst possible hazard.
autions: If combined with other psy-
tropics or anticonvulsants, consider
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ed; drugs such as phenothiazines,
otics, barbiturates, MAO inhibitors
other antidepressants may potentiate
ction. Usual precautions indicated in
ents severely depressed, or with latent
ression, or with suicidal tendencies.
Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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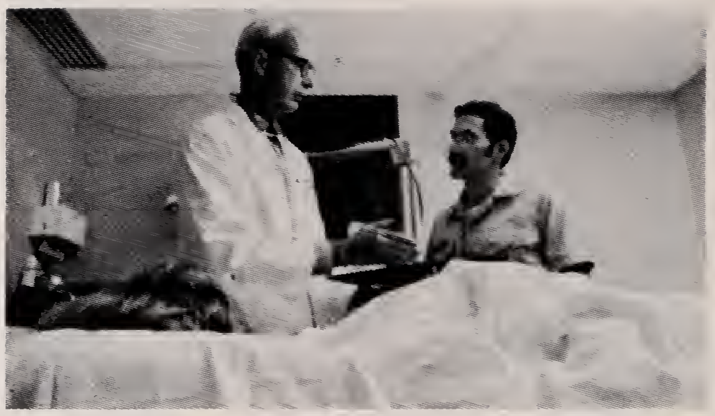

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President's Letter

Health Planning Law (PL. 93-641)

The AMA has left no doubt about its conviction that the new Health Planning Law (PL. 93-641) is unconstitutional and threatens to create serious harm to the Health Care System. The concern is so great that the AMA has requested permission to join with the State of North Carolina in a legal suit to determine the constitutionality of the act. The impact of this law came to the forefront in Minnesota this past month in two significant areas—Provider Representation of HSA Boards and Certificate of Need requirements. Before I discuss the specifics let me reflect back two years and review what happened while we physicians were absorbed in our day-to-day problems.

Congress passed the Health Planning Act of 1974. This law is not just another Governmental Abstraction. It's not just a rehash of Comprehensive Health Planning, Regional Medical Programs and so forth. Quite to the contrary, it's the framework for a Bureaucratic Totalitarianism that could reshape the health care system as we know it . . . including the responsibilities and expandability of hospitals and other facilities and even the rates they charge. Also, moves to put doctors' offices and fees within the scope of the act are afoot in the Department of HEW even though the AMA had them excluded from the law. As we have seen with PSRO legislation—regulations are easily written which go beyond the original intent of the law and we expect more of the same with this law.

Consider some of the ways, however, in which the Health Planning Act would flout the principles of rational planning, be a heavy expense in itself, imperil the quality of CARE—all planned and expedited with minimal input from the providers of Health Care in this country.

The secretary of HEW is to dominate the somewhat overlapping levels of Federal, State and Local authority. He is also to issue National Health Planning Policy; appoint a National Advisory Council; approve State and Local Planning Agencies and the funds they receive, and establish the criteria and procedures they use.

Certificate of Need Legislation with minimum requirements must be adopted in all States, as prescribed by the HEW secretary. The need for all existent institutional services must be reviewed every five years; the need for all new institutional facilities and services must be certified. Practice-profile data from PSROs, plus the minority status of direct providers of care on local planning boards could arbitrarily influence the expansion of continuation of services.

Six states are to get Federal Grants to demonstrate rate regulations for health services. This could become mandatory for all states and encompass physicians, if various planners get their way. The result of regulation is likely to be an obsession with cost at the expense of high quality care.

How has all the preceding affected us to date. Dr. John Coleman* provided the early warning system with his Physician's Metropolitan Health Force which is now a part of the New Division of Socio-economic Affairs of the MSMA. Dr. Coleman sought adequate representation on local planning boards, appeared at public hearings pursuant to the law, and fought the great potential danger as if there was no other game in town. What alarms me is the end result of our first encounter. In the Twin City area we have an HSA board of thirty members which deals primarily with the health of residents within a seven county area in Minnesota and has only one representative from the practicing physician community. Hennepin County, which now has two-thirds of all physicians within this area is not represented on the Health Board at this time. We feel this a gross injustice of the system, and it does place a great deal of stress on the relationship between the physician community and the Health Board/ Council. Our deepest concern is the operational procedures employed by the Metropolitan Council which is the Health Systems Agency for Health Service Area Five in Minnesota. These involve two specific areas . . .

---

*See page 576.

1. The legal relationship between the health board and the council, and the autonomy under which the health board will be allowed to function as the separate governing body for health planning.
2. The adequate representation of the physician community on the metropolitan health board, and the appointment process whereby those provider members are selected.

We have long been aware of the current authority granted to the Metropolitan Council under State statute. However, since the HSA is an arm of the Federal Government and since the funds are provided under a Federal Program, we feel that the Health Board, which is the entity comprised of providers and consumers, should have more control and final decision making authority over all Health matters. It is only through the adequate input of the providers and consumers on the health board that acceptable health planning decisions can be made in our area. If these decisions are allowed to be overturned by the appointed members of the Metropolitan Council, as they were when the physicians and the Health Board's Recommended Physicians' Representatives were not re-appointed, then the credibility of this body and the productivity of the HSA within the metropolitan area will be severely threatened. The physician community hopes to maintain a close working relationship with the Health Board. We both have many of the same objectives in mind. However, if the council has the ultimate authority in over-turning all health decisions and if the selection process and representation of the physician community is not both equitable and allowed to originate at the physician community itself, then we will work to see that the one-year conditional designation for the Health Board/Council will not receive final approval.

The other significant area in relation to our new health planning laws arose when the Minneapolis Clinic of Psychiatry and Neurology was notified by the Minnesota State Board of Health of their intent to hold a hearing on July 6, 1976 on the Clinic's "Notice of intent" to purchase a tomographic scanner. The request for the hearing originated from the Metropolitan Council and Health Board. It was the first hearing of this nature in Minnesota since the adoption by the legislature of the certificate of need requirement in Minnesota Statute 145.76 and the State Board of Health policy and procedure number PA-4 (61076). It will be recalled that the association was successful in eliminating physicians' offices from the certification of need. The statue does require a physicians' office to file a letter of intent with the State Board of Health for any purchase of equipment over $100,000. If the State Board of Health believes there may be a circumvention of the certificate of need requirement through a collusion by the physician's office and hospital, a hearing may be held . . . but only to determine whether or not a physician's office and hospital have acted in collusion to circumvent the certificate of need law. It was extremely surprising to us that the Metropolitan Council even requested this hearing in the absence of any documentation or evidence of a collusive arrangement. In fact, after the evidence and materials were presented, just the opposite was the case. The Association testified at the hearing in support of this view. The Hearing Officer will submit his recommendations to the State Board of Health the end of July on this case, and your Association will continue to follow this matter closely. We must maintain our strong opposition to the application of "certificate of need" to physician's offices.

For the moment, there is no other game in town.

RE Anonsen

Richard E. Anonsen, M.D.
President
Minnesota State Medical Association

Editor's Notebook

Health Care 1976: The View From Boston. Part I

> *"For mercy's sake, gentlemen, let us have a little less science and a little more art!"*
>
> *Trousseau*
> *Lectures on Clinical Medicine*
> *Paris, 1868*

I am writing this from a small dormitory room on the Harvard Business School campus.

What am I doing here? And why?

Well, fifty-three other "health care professionals" and I are here for a six-weeks course on Health Systems Management. The Harvard School of Public Health, the Harvard Business School, and the Harvard Medical School jointly give the course. Its purpose, says the introductory booklet, is: ". . . to enhance the skills and to broaden the perspective of senior health professionals." I am also here so I can better explain what's going on in the Health System to the private practitioners of medicine, who, after all, take care of most patients.

Students

We are now ending our second week. So far, the course's skill-enhancing value remains in doubt. But there is no question the course broadens perspectives. The makeup of the student body and faculty make this inevitable. Students come from 17 states and eight countries and include 60 percent physicians. Most of these are from academic, administrative, and governmental positions. This proportion of M.D.s is the greatest in the five-year history of the course. The first class had 20 percent physicians. Non-M.D.s are top level managers in the health field: business executives, government officials, hospital administrators and consultants. Even a third-party representative is here.

Faculty and Curriculum

The faculty teach Health Economics, Marketing Development, Legal Liability and Responsibility, Labor Relations, Management Control, Management of Operations, Health Services, Organizational Issues, Financial Management, and Health Policy. The professors are excellent, and are genuinely pleased that more physicians each year choose to steep themselves in managerial lore.

Private Sector

I am one of the few from the private sector of medicine. I think this is so for three reasons: (1) not many physicians can take six weeks off; (2) to qualify, you have to be in an administrative position, and; (3) a large organization has to sponsor you. The Minnesota State Medical Association and the Metropolitan Medical Center, where I am a pathologist, are sponsoring me (at my expense).

Postamble

So much for the preamble.

This being Boston and tomorrow being the Fourth of July 1976, the eve of this Nation's 200th birthday is an appropriate place and time to give a view of the Health Care System. Incidentally, the Swedish physician attending this course, Bengt Mollstedt of Gothenberg, informed me the other day that Sweden had been working on their Health System for nearly 300 years, so he has hopes for the Americans, particularly Minnesotans, many of whom after all, are of Swedish origin.

Costs

Questions of exploding medical costs—why they are rising, how to contain them, and what system they are leading to—fill the air here. This cost surge exists worldwide. Other countries, no matter what their system, have similar health inflation problems. Every society, it seems, demands better health services, and this demand drives costs up.

Regulation

One thing that differs about America is our elaborate and inefficient regulatory apparatus to contain costs. In our country, with its pluralistic society and welter of multiple regulartory organizations, it is no small trick to control costs, improve health, and widen access—all at the same time. The regulatory situation has led to a kind of schizophrenia between government planners and physicians.

Planners and Physicians

The planners, faced with limited resources and looking at society as a whole, are saying physicians must analyze more closely the economic consequences of their acts. The government looks at the large number of dollars and "average patients" and insists on accountability for public money.

But the physicians, faced with patients who demand the latest in technology, must consider individuals. As one of our instructors pointed out: "When it comes to me, forget the costs. Cut the costs for the rest of the people, but for me the sky's the limit." Government officials and physicians have a hard time understanding each other's logic. Each resents the other's attitudes, rubs the other wrong, and suspects the other's motives. Yet each depends on the other.

Technology

A second major issue here, closely related to costs, is Technology (with a capital "T"). Make no mistake about it. Planners blame physicians for using too much costly Technology too quickly without first using clinical trials to measure statistical clinical yield.

Two commonly sited examples are: coronary bypass surgery and brain scans by computerized axial tomography (the so-called CAT scanner). The critics' arguments run like this: (1) coronary bypass surgery costs society at least $10,000, yet we have no randomized clinical studies showing these bypasses prolong life. Or (2) as of December 1975, 340 CAT scanners, at the yearly operating cost of $500,000, were on order in this country, yet it is not clear the CAT's diagnostic information leads to a better average outcome for society. So goes the logic of those who are measuring the health of society rather than treating the illnesses of individuals.

National Health Insurance

In closing, I shall add a word or two about National Health Insurance. Most participants here feel National Health Insurance, though perhaps inevitable, is not imminent, probably not for three to five years. The cost of Medicare and Medicaid, ten years old this week, frightens these people and makes them skeptical and suspicious of the Government's ability to provide economic care for everybody. This year's expenditures for national health will top 130 billion dollars, compared to under 40 billion in 1965. This costly experience leads many of these professionals to take a go-slow, think-it-through attitude before plunging into national comprehensive coverage. If National Health Insurance comes, it will come in stages.

Richard L Reece MD

Editor-in-Chief

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Contents—August, 1976

Volume 59:8
Pages 507-586

OVER PAINTING—"William H. Mayo, M.D., Surgeon"
Louis A. Buie, Sr., M.D. 556

RESIDENT'S LETTER—Health Planning Law (PL. 93-641)
Richard E. Anonsen, M.D., President 511

DITOR'S NOTEBOOK—Health Care 1976: The View from Boston. Part I
Richard L. Reece, M.D., Editor-in-Chief 513

RIGINAL CONTRIBUTIONS

Presurgical Coagulation Testing
John O. Swanson, M.D. 517

Esophageal Moniliasis
John N. Mork, M.D. et al. 523

The Calorie Intake of Patients with Advanced Cancer
Athanasios Theologides, M.D. et al. 526

Current Status of the Radioactive ^{131}I Uptake Test
Robert H. Caplan, M.D. et al. 530

The Spectrum of Agricultural Medicine
Richard W. Rasmussen, M.D. and George A. Cole, M.D. 536

The Aging Eye
F. C. Wuest, M.D. et al. 540

DITORIALS

Omphaloskepsis and Other Umbilical Phenomena
Richard L. Reece, M.D., Editor-in-Chief 551

Spectrum of Agricultural Medicine
Henry Bauer, Ph.D. 552

"Silent Thyroiditis" Versus Thyrotoxicosis Factitia
Colum A. Gorman, M.B., B.Ch 552

Caloric Intake of Patients with Advanced Cancer
Neil Hoffman, M.D. 553

Laboratory Tests in Coagulation Screening
N. D. Kostich, M.D. 555

Uterine Prolapse and Upper Urinary Tract Obstruction
Bruce E. Linderholm, M.D. 555

ETTER TO THE EDITOR—Twenty-Five Years Association of a Psychiatrist
Irving C. Bernstein, M.D. 556

IEALTH POLICY—A Challenge—Health Care Cost Containment
G. Roy Diessner, M.D., Past President 557

IISTORY—Sister Mary Joseph's Nodule and Its Relationship to Diagnosis f Carcinoma of the Umbilicus
Jack D. Key, M.A., M.S. et al. 561

EDIATRICS—A Look at Child Health Manpower in Minnesota
Steven G. Thompson 580

PECIAL ARTICLE—Coronary Vein Perfusion
Jack Kolff, M.D. and W. J. Kolff, M.D. 589

IINNESOTA STATE MEDICAL ASSOCIATION—Annual Meeting
R. D. Semsch, M.D. 560

ISMA HIGHLIGHTS—Physician's Health Forces—Let's Get Involved 576

ONTINUING MEDICAL EDUCATION 514-A, 525, 529, 535, 559

LASSIFIED ADVERTISEMENTS 575

NDEX TO ADVERTISERS 586

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Presurgical Coagulation Testing

JOHN O. SWANSON, M.D.*

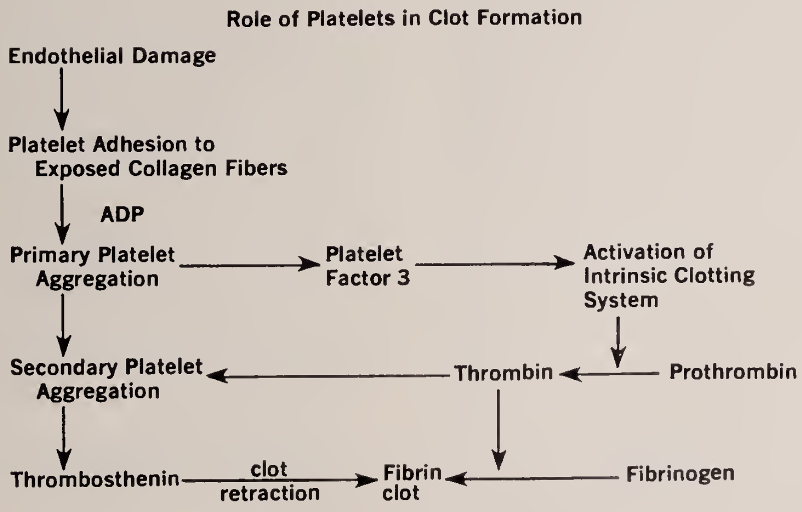
A complete medical history is the first step in a preoperative coagulation evaluation. Common laboratory tests detect most potential clinical bleeding problems. A clotting test profile is presented in this article, followed by seven case illustrations.

NORMAL CLOTTING DEPENDS upon the interaction of blood vessels, platelets and plasma clotting factors. Most clinical coagulation problems are the result of a defect in either the platelets or the plasma coagulation system.

When a blood vessel is severed, the vessel wall constricts and circulating platelets adhere to the exposed collagen fibers (Figure 1). Several substances are then released from platelets, including adenosine diphosphate (ADP) which promotes the cohesion and aggregation of additional platelets and the production of platelet factor 3, which is essential for the intrinsic plasma coagulation system.[1] A secondary irreversible aggregation follows, aided by thrombin, with further release of platelet factors. The platelet plug is later reenforced by the fibrin clot. Thrombosthenin, another product of platelet aggregation, causes retraction of the fibrin clot.

The plasma clotting diagram (Figure 2) is a modification of diagrams by Yale Nemerson[2] and J. R. Edson.[3] When factor X is activated by either the intrinsic or the extrinsic pathway, this factor, in conjunction with activated factor V, calcium, and platelet factor 3, converts prothrombin to thrombin. Thrombin then converts fibrinogen to fibrin monomers and also autocatalyzes the intrinsic reaction. Following fibrin polymerization, factor XIII stabilizes the fibrin clot.[1-3]

The formation of fibrin is associated with activation of the fibrinolytic system, which prevents indefinite clot formation. The precursor plasminogen is activated to plasmin by tissue and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Platelet Factor 3
Activation of Intrinsic Clotting System
Secondary Platelet Aggregation
Thrombin
Prothrombin
Thrombosthenin
clot retraction
Fibrin clot
Fibrinogen

Figure 1

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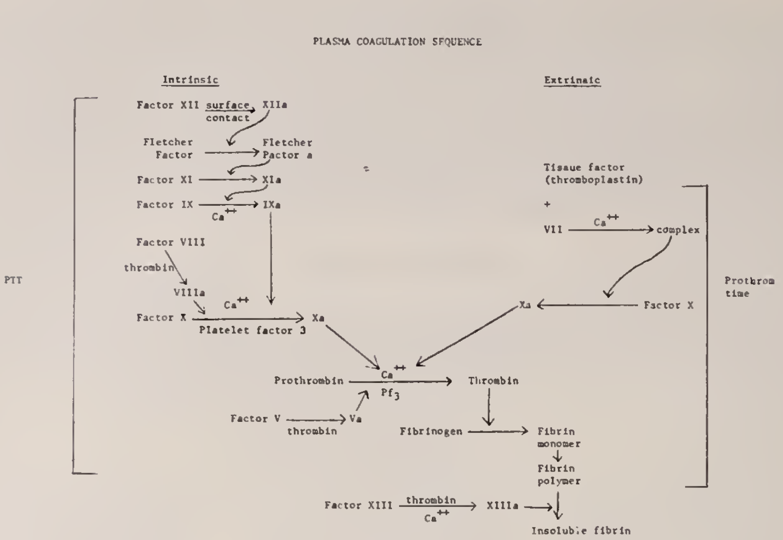
*Pathologist, Metropolitan Medical Center, Minneapolis, Minnesota.

See editorial, page 555.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Factor X
Xa
Platelet factor 3
PTT
Tissue factor (thromboplastin)
+
VII
complex
Factor X
Xa
Prothrom time
Prothrombin
Thrombin
Pf3
Factor V
Va
thrombin
Fibrinogen
Fibrin monomer
Fibrin polymer
Factor XIII
XIIIa
Insoluble fibrin

Figure 2

plasma activators and by thrombin. Plasmin cleaves the fibrin clot; it also inactivates factors V and VIII.[1,4]

Medical History

A careful, thorough patient history is indicated before a single laboratory test is performed.[5] Most congenital clotting problems are evident in the history. Some mild congenital defects and many acquired bleeding problems may be asymptomatic. Unfortunately, the patient with a mild bleeding disorder often needs the most extensive coagulation work-up to diagnose the difficulty.[6]

Specific findings in the history and physical examination include petechiae, easy bruising excessive bleeding from cuts and abrasions, mucous membrane bleeding such as nosebleeds and gastrointestinal bleeding, hemarthroses, menorrhagia and postpartum hemorrhage.[7,8] There may have been unusual bleeding at the time of previous surgery, especially dental surgery or adenotonsillectomy. Sometimes bleeding abnormalities are apparent in the newborn following circumcision or with umbilical stump hemorrhage.[4,9]

Associated illnesses should alert one to the possibility of acquired coagulation defects—a diminution of plasma coagulation factors (except VIII) with liver disease, interference with the interaction of the clotting factors in dysproteinemia, impaired platelet function in uremic patients, or the presence of precipitating causes for disseminated intravascular coagulation.[7]

A family history of unusual bleeding is also important, especially involving the parents, siblings and children of the patient.

Finally, one should question the patient about medications. This history must include nonprescription items. Aspirin and aspirin-containing compounds have a seven to ten day adverse effect on platelet aggregation and the bleeding time.[9-11] Other medications which affect platelet function include antihistaminics, anti-inflammatory medications, barbiturates, some tranquilizers, chloral hydrate, dilantin, steroids, reserpine, atropine and volatile general anesthetics.[11-13]

Coagulation Profile

Subsequent to a complete medical history, the following tests are suggested for presurgical coagulation screening:

1. The *prothrombin time* (Quick) monitors the extrinsic system and identifies deficiencies of fibrinogen, prothrombin and factors V, VII, and X.
2. The *activated partial thromboplastin time* (aPTT) detects significantly decreased levels of all plasma clotting factors except factors VII and XIII.[7] It is the primary screening test of the intrinsic system and identifies hemophilioid disorders. The *aPTT* is sensitive to the effect of heparin,[3,14] but does not reflect the level or activity of platelet factor 3.
3. The *thrombin time* is added to detect hypofibrinogenemia and circulating plasma anticoagulants such as heparin, fibrin split products, and unclassified anticoagulants which may occur in systemic immunological disorders.[5]

4. *Platelet count.* Bleeding may result from either an elevated or a decreased platelet count.[15] If the platelet count is less than 100,000/cu. mm. excessive bleeding may occur with major surgery.[16] Patients with platelet counts under 10,000 to 20,000/cu. mm. are prone to serious spontaneous bleeding.
5. A *blood morphology* identifies thrombocytopenia secondary to a blood dyscrasia as a possible cause of bleeding. In addition, myeloproliferative platelets and other platelet morphology aberrations may be seen. Red cell fragments are characteristic of disseminated intravascular coagulation. The platelet count estimate from a peripheral smear tends to verify the platelet count.[4,5]
6. The *Ivy bleeding time* evaluates platelet function and the integrity of blood vessels. Harker and Hathaway have found the bleeding time to be an accurate test of most functional platelet defects.[17,18] This test is also abnormal in most instances of von Willebrand's disease.[15,19,20] The template modification of the Ivy bleeding time described by Mielke[21] is preferable to the standard bleeding time.
7. *Clot retraction and clot lysis.* In our laboratory, two additional clot tubes are drawn from the patient. One is kept at room temperature and evaluated qualitatively for clot retraction after 24 hours. The clot is either firm and elastic (normal) or soft and friable (abnormal). The other tube, incubated at 37 C, is assessed for semi-quantitative clot retraction at one hour and for retraction and clot lysis after 24 hours.

   The clot retraction test is helpful in detecting some functional platelet disorders. A soft, poorly-retracted clot with numerous free red cells in the bottom of the test tube frequently indicates drug-induced platelet dysfunction, most often related to aspirin ingestion.

   Clot lysis evaluation is of minimal value but is easy to perform when observing the incubated tube. The euglobulin clot lysis test is indicated when there is a question of primary fibrinolysis a rare condition.[9]

Interpretation

If the prothrombin time is abnormal and the other survey tests, including the activated partial thromboplastin time, are normal, a factor VII deficiency should be suspected, since factor VII is the one plasma clotting factor needed only for the extrinsic system (see Figure 2). A deficiency of factor V, X, prothrombin or fibrinogen results in both an abnormal activated partial thromboplastin time and an abnormal prothrombin time. A normal prothrombin time and an abnormal aPTT suggest a deficiency of factor VIII, IX, XI or XII.

An isolated prolonged thrombin time is unusual, ordinarily a low fibrinogen level is detected by a prolonged prothrombin time and a prolonged aPTT.

If the activated partial thromboplastin time and the Ivy bleeding time are the two abnormal findings in the profile, von Willebrand's disease should be considered. However, patients with von Willebrand's disease seldom have a factor VIII level sufficiently depressed to prolong the aPTT. More often this individual has an isolated prolonged bleeding time on the coagulation profile.

In thrombocytopenia, clotting tests which reflect platelet activity are abnormal. Harker and Slichter found a direct inverse relation between the bleeding time and platelet count when the latter ranged from 100,000 to 10,000/cu. mm.[17] The bleeding time may also be prolonged in patients with high platelet counts resulting from a myeloproliferative disorder.[15,22]

If the platelet count is normal and the bleeding time and clot retraction tests are abnormal, one would suspect a qualitative platelet disorder. If the Ivy bleeding time is the only abnormality in the profile, the patient may have von Willebrand's disease, platelet dysfunction or increased vascular fragility.[15] An isolated abnormal clot retraction denotes ineffective platelet function and may be associated with drug ingestion.

In patients with disseminated intravascular coagulation, most or all of the tests in the coagulation profile may be abnormal.

Case Studies

Case 1

A 58-year-old male was admitted for exploratory renal surgery. Five month history of hematuria and nosebleeds. Patient and family history for bleeding otherwise negative. No medications.

Coagulation Profile

Prothrombin time—22.0 seconds (control 12.0 seconds)

aPTT—33.1 seconds (control 35.0 seconds)

Thrombin time—15.7 seconds (control 15.0 seconds)

Blood morphology, platelet count, Ivy bleeding time, clot retraction and clot lysis all within normal limits.

Repeat prothrombin time—30.0 seconds (control 12.0 seconds)

Initial Impression

Isolated factor VII deficiency.

Additional Coagulation Reference Laboratory Data

Quantitative fibrinogen—450 mg/dl.

Factor assays V, (VIII, IX), X and prothrombin all within normal limits.

Factor VII assay 3% of normal.

Patient's two sons had normal prothrombin times but factor VII assays were 46% and 55%, implicating them as carriers of factor VII deficiency.

Diagnosis: Isolated congenital factor VII deficiency.

Comment

Many cases of isolated factor VII deficiency reported in the literature have had bleeding symptoms much earlier in life than our patient.[23,24]

Case 2

A 17-year-old female was admitted for a tonsillectomy. Negative patient and family history for bleeding. No drugs.

Coagulation Profile

aPTT—greater than 75.0 seconds (control 32.3 seconds)

Remainder of coagulation profile within normal limits.

Initial Impression

Deficiency of a factor needed only for the intrinsic pathway. (Normal prothrombin time rules out deficiencies of fibrinogen, prothrombin, and factors V, VII, and X).

Additional Coagulation Reference Laboratory Data

Factor XII assay—less than 1%

Patient's mother had a normal aPTT, but her factor XII level was 40%, indicative of a carrier state.

Diagnosis: Congenital factor XII deficiency.

Comment

Patients with factor XII deficiency seldom have clinical bleeding problems.[1,7]

Case 3

A 22-year-old male presented with a long history of excessive bleeding. First massive bleed occurred after a tooth extraction, age 5. Many subsequent bleeding episodes in the muscles and joints. Previously diagnosed factor V deficiency. Family history negative.

Coagulation Profile

Prothrombin time varied from 41.0 to 87.8 seconds (control averaged 12.0 seconds).

aPTT—70.0 seconds (control 35.0 seconds)

Ivy bleeding time—21 minutes

CBC, morphology, platelet count, clot retraction and clot lysis all normal.

Diagnosis: Congenital factor V deficiency.

Comment

The prolongation of both the prothrombin and the partial thromboplastin times is consistent with factor V deficiency. Bowie notes that the bleeding time, although normal in most plasma factor deficiencies, may be prolonged in factor V deficiency and hypofibrinogenemia.[15]

Case 4

A 55-year-old male was admitted for femoral-popliteal bypass graft. Patient and family bleeding history were negative. No history of drug ingestion. A coagulation profile was ordered after blood bank technologist noticed that a cross-match tube was slow to clot.

Coagulation Profile

Prothrombin time—13.7 seconds (control 12.6 seconds)

aPTT—80.6 seconds (control 39.6 seconds)

Thrombin time—14.3 seconds (control 14.2 seconds)

Platelet count—184,000/cu. mm.

Ivy bleeding time—6 minutes

CBC, morphology, clot retraction and clot lysis—normal.

Since the history was negative in a 55-year-old man, one might suspect an acquired disorder. A normal thrombin time excluded the presence of heparin.

Reference Laboratory Data

Factor Assays:

VIII— 59%

IX — 70%

XI — 77%

XII —110%

Factor VIII is mildly depressed but does not account for the abnormal aPTT. The aPTT and the prothrombin time are prolonged only when a deficient factor is less than about 30% of normal.[2]

In cases of simple factor deficiency, adding normal plasma to the patient's plasma should correct the abnormality. An inhibitor or an inactivator (antibody?) to a plasma clotting factor will inhibit or inactivate the involved factor from a normal individual as well as that from a patient, and thus the PTT is not corrected by normal plasma.[2,7] An inhibitor produces prolongation of the PTT of normal plasma without incubation, while an inactivator requires an incubation period for its effect to be manifest.[11] In patient #4, the activated PTT did not change with an equal mixture of patient and normal plasma before incubation. The PTT became further prolonged after a two hour incubation, implicating both an inhibitor and an inactivator.

Diagnosis: PTT inhibitor, perhaps secondary to lupus erythematosus, and a probable anti-factor VIII antibody.

Case 5

A 39-year-old female was evaluated because of postoperative bleeding following an abdominal hysterectomy.

Coagulation Profile Abnormalities

Ivy bleeding time—greater than 10 minutes

Friable soft clot after 24 hours incubation at 37 C

Remainder of profile was normal.

Coagulation studies at the reference laboratory substantiated the impression of abnormal platelet function, with demonstration of abnormal platelet aggregation and abnormal platelet morphology.

The patient and family bleeding history were negative, but the patient had been taking aspirin and an antihistaminic regularly for many months prior to her surgery. Several weeks after discontinuing these medications, the patient had a completely normal coagulation profile and later gallbladder surgery was uneventful.

Diagnosis: Drug induced platelet dysfunction.

Comment

This case is illustrative of many who have impaired platelet function secondary to drug ingestion, particularly aspirin-containing compounds. Usually, platelet function abnormalities are indicated by abnormal platelet aggregation and platelet factor 3 studies[13] (Figure 1).

Case 6

A three-year-old male child presented with sudden onset of gross hematuria. No history of previous bleeding. Patient's paternal aunt is a "bleeder." The patient was taking antibiotics and aspirin for an upper respiratory infection.

Coagulation Profile

Bleeding time—greater than 10 minutes.

Remainder of the profile. including the aPTT, was within normal limits.

Coagulation Reference Laboratory

Substantiated the initial impression of von Willebrand's disease by demonstrating a markedly abnormal platelet adhesiveness test and a borderline factor VIII level. Platelet aggregation studies showed the effect of aspirin (abnormal secondary aggregation).

Diagnosis: von Willebrand's disease.

Comment

Von Willebrand's disease is characterized by some or all of the following: a prolonged bleeding time, an abnormal platelet adhesiveness test, and/or a decreased factor VIII level.[19,25,26]

In Case #6, neither von Willebrand's disease nor aspirin ingestion adequately explained the hematuria and a complete renal investigation was carried out.

Case 7:

An 83-year-old diabetic female was admitted because of a fractured shoulder and gangrene of the right foot. There were extensive ecchymoses in the fracture area. Negative history.

Coagulation Profile

Prothrombin time—23.2 seconds (control 11.7 seconds)
aPTT—greater than 120 seconds (control 32.4 seconds)
Thrombin time—26.8 seconds (control 14.2 seconds)
Platelet count—60,000/cu. mm.
Ivy bleeding time—greater than 10 minutes
Clot retraction and clot lysis—80% retraction in one hour. Poor clot formation. No lysis.
Morphology—numerous red cell fragments.

Additional Coagulation Studies

Fibrin split products (semiquantitative)—greater than 40 ug/ml. (definitely elevated).
Quantitative fibrinogen—59 ug./dl.

Diagnosis: Disseminated intravascular coagulation, probably secondary to bacteremia.

All coagulation studies returned to normal after three days of intravenous heparin therapy and antibiotics. Blood and wound cultures grew Clostridium perfringens.

Comment

When disseminated intravascular coagulation (DIC) is suspected, the fibrin split products test and a serum fibrinogen level are added to the coagulation profile. The peripheral smears are carefully searched for the presence of fragmented erythrocytes. Factor VIII and factor V assays may be added.

The consumption of platelets and plasma clotting factors in the intravascular clotting process is reflected in abnormal coagulation profile tests. Fibrin, fibrinogen, and factor V and VIII levels may also be reduced by circulating fibrinolysins which are increased in response to widespread clotting. Fragmentation of red cells is apparently caused by blood flow through capillaries narrowed by the intravascular clotting process.

Fibrin split products/fibrinogen degradation products are breakdown molecules of fibrin and fibrinogen resulting from the action of fibrinolysins. Serum levels of fibrin split products are almost always elevated in DIC. Sun and associates found that the fibrin split products (FSP) test was abnormal more often than other coagulation tests in patients with DIC secondary to cancer.[27] The FSP test is not specific; serum levels may be increased in pulmonary infarction, deep vein thrombosis, myocardial infarction and other clinical conditions.

Cooper, Bowie and Owen have explained the variation in test results seen in the DIC syndrome.[28] They write of decompensated, compensated and overcompensated disseminated intravascular coagulation, depending on whether fibrinogen and platelets are decreased, within normal limits, or increased as a result of liver and bone marrow attempts to replenish these elements.

Discussion

After exclusion of patients who are on anticoagulant therapy, we have experienced a predominance of the following coagulopathies, in decreasing order of incidence:

1. Platelet dysfunction many drug-induced;
2. Von Willebrand's disease;
3. Acquired multiple factor coagulopathies (a) Prothrombin complex deficiencies; (b) Disseminated intravascular coagulation; and
4. Isolated congenital factor deficiencies.

Sanfelippo and Hussey found that a qualitative platelet disorder was the most common coagulopathy they encountered.[29] Edson states that "drug-induced platelet dysfunction is a much more important cause of actual bleeding than we have realized."[11]

Functional platelet problems are difficult to categorize.[15] For this reason, patients with evidence of abnormal platelet function on our screening profile are referred to a coagulation reference laboratory for a platelet adhesiveness test, platelet aggregation studies and platelet factor 3 assay. An additional and more available platelet function test is the prothrombin consumption test, which indirectly evaluates the intrinsic plasma clotting mechanism up to the point of prothrombin conversion to thrombin.[30] In contrast to the aPTT, the prothrombin consumption test may detect a deficiency of platelet factor 3.[6]

Examples of the common coagulopathies have been previously discussed with the exception of one important group: those with acquired prothrombin complex deficiencies. After excluding those on anticoagulants, many patients with prolonged prothrombin times have liver or biliary tract disease. The aPTT and the thrombin time are also prolonged in these conditions, since all plasma coagulation factors except factor VIII are produced in the liver.[2] Occasionally, abnormal prothrombin and partial thromboplastin times are secondary to malabsorption or prolonged oral antibiotics with inadequate food intake. Vitamin K absorption is then decreased and the prothrombin complex factors (prothrombin, VII, IX, X) are not produced in adequate quantity.[7]

When consultation is requested, we usually suggest the complete coagulation profile prior to extensive major surgery and for preoperative evaluation of patients with a personal or family history of unusual bleeding. If any one of the profile tests is abnormal, a more extensive evaluation may be indicated, often with the help of a reference laboratory for specialized procedures such as platelet function tests and factor assays.

When physicians request coagulation screening for a patient with a negative bleeding history prior to less formidable surgery, a simpler and usually adequate profile consists of an Ivy bleeding time, an aPTT, and a complete blood count with blood morphology. This group of tests should detect some qualitative and quantitative platelet defects, von Willebrand's disease and plasma clotting deficiencies except factors VII and XIII.

We discourage use of the "routine bleeding and clotting time." The capillary clotting time is obsolete and the Lee-White clotting time is insensitive.[4,31] Better tests are available.

Summary

A coagulation profile has been presented to aid in presurgical evaluation. The tests included are the prothrombin time, activated partial thromboplastin time, thrombin time, platelet count, blood morphology, Ivy bleeding time, clot retraction and clot lysis. This profile, along with a careful history, should uncover most significant clotting problems prior to surgery. Additional coagulation studies may be required to identify a precise abnormality.

I wish to thank Doctor J. R. Edson and Doctor C. M. Strand for reviewing this paper and making helpful suggestions.

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15-31. Will be found on page 559.

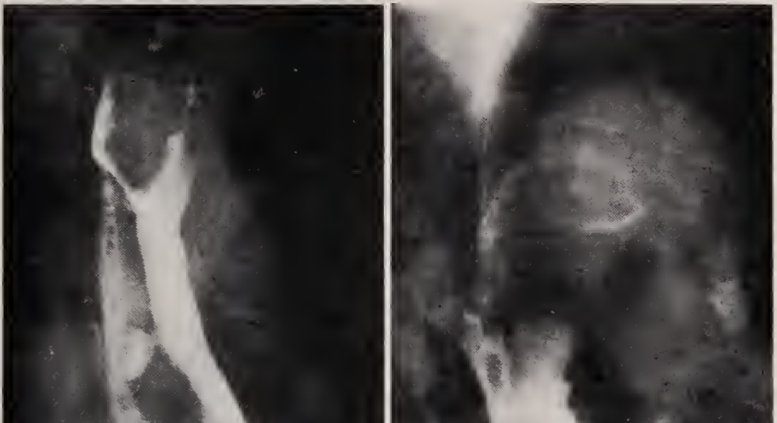
Esophageal Moniliasis

Unusual X-Ray and Endoscopic Findings

JOHN N. MORK, M.D.;* MILTON W. PLUCKER, M.D.* and
EUGENE J. BIRKEMEYER, M.D.*

An 89-year-old lady had an excellent response to oral nystatin suspension for esophageal moniliasis. The clinical picture of acute chest pain in an otherwise healthy individual is atypical. Unusual Xray and endoscopic findings are described.

ESOPHAGEAL MONILIASIS, considered quite rare with only 70 cases reported through September 1970, is being reported with increasing frequency. The usual patient is debilitated by another illness or by treatment of another illness especially with antineoplastic drugs, steroids or



Figures 1(a) and (b)—(1a-left) Esophagogram of 12-3-74 demonstrating extensive irregularity of the esophageal mucosa, large indentations of the esophageal lumen and apparent multiple fistulae. (1b-right) Repeat esophagogram of 12-13-73 demonstrating nearly complete resolution of the original findings.

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antibiotics. Esophageal moniliasis is usually curable by an oral suspension of nystatin.

Our case differs from the usual. The unusual features are: (1) good general health of the patient (2) acute chest pain as the presenting symptoms (3) atypical Xray and endoscopic findings.

Case Report

An 83-year-old housewife was admitted to Worthington Regional Hospital in November, 1973 complaining of sudden pain in the epigastrium radiating into the substernal area. This occurred shortly after breakfast. The patient had been having some dysphagia for approximately six months preceding admission.

She was in moderate distress. Her pulse rate was 100 and the blood pressure 230/100 mmHg. Temperature: 96.8° Cardiac examination was unremarkable.

Examination of the abdomen revealed tenderness in right upper quadrant and in mid epigastrium. There was no rebound tenderness nor guarding. Because of the sudden onset and location of the pain, the patient was admitted to the coronary care unit.

Laboratory Studies

Hemoglobin, white blood count, differential unremarkable. Urinalysis: 1+ glucose. Sed rate 8 mm. per hour. SGOT and CPK were normal on 11-27 and 11-28-73. A fasting blood sugar was 109 mg%. The serum bilirubin was elevated at 2.1 mg%, with a direct reacting fraction of 0.3 mg%. EKG showed only nonspecific ST-T changes on four separate studies. Chest Xray was negative except for thickened pleura in the right costophrenic angle.

Upper GI series (Figure 1a) demonstrated irregular mucosa with large indentations and multiple fistulae involving the esophagus from above the aortic arch to near the esophago-gastric junction. The extent of involvement and the clinical symptoms favored chronic inflammatory masses such as mycosis or secondary involvement from mediastinitis. Esophagoscopy was performed on 12/6/73. At the level of 15 cm. from the teeth there was a yellow-white cobbled exudate adherent to the wall of the esophagus. At the 25 cm level there was a mass lesion along the right side (Figure 2). The lesion obstructed the lumen of the esophagus, was friable and bled easily. There were areas of erythema of the mucosa proximal to this mass. Biopsies were taken from the edge of the mass lesion and from the mucosa proximal to the lesion. The visual endoscopic findings were interpreted as a neoplasm of the esophagus with associated moniliasis. The patient was started on nystatin suspension 1 cc. tid by mouth. Subsequently, biopsies showed acute and chronic inflammation with granulation tissue. Methenamine silver stain for fungi failed to reveal monilial hyphae.

Six days after starting the nystatin treatment, an esophagogram (Figure 1b) was nearly normal. The patient related that the dysphagia was gone. She was discharged on nystatin suspension and has continued to do well. Her blood pressure elevation relented without specific treatment.

Discussion

Monilial esophagitis has been reported in patients of all ages.[5] Most have been caused by C. albicans and a few by other Candida species.[1,5] Dysphagia is the major symptom and may or may not be painful. Few cases of monilial esophagitis have been reported but the disease is common enough in an oncology practice that many are treated empirically with nystatin suspension for dysphagia.

Several authors[1-5] report that monilial esophagitis occurs most commonly in patients with decreased host resistance from illness or medication.

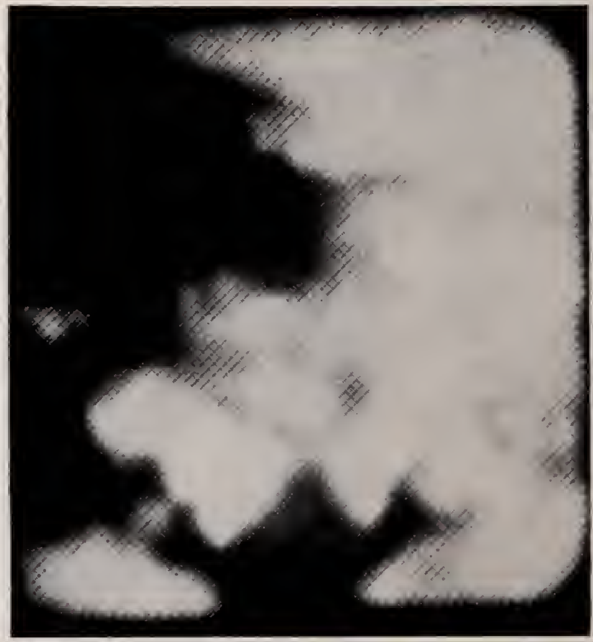

Fig. 2—Endoscopic photograph of the esophagus demonstrating a mass lesion with yellow exudate on the surface of the mass and on the mucosal surface adjacent to the mass. The esophageal lumen is seen in the upper left hand corner. The hemorrhagic area in the left lower corner is the site of a mucosal biopsy.

The only adverse factor in our patient was her advanced age of 83 years. A previously reported case[1] also occurred in an otherwise healthy 89-year-old lady. Recently, monilial esophagitis was reported in an otherwise healthy young man who was taking Tetracyline for a respiratory infection.[9] Thus monilial esophagitis can be the cause of dysphagia in otherwise healthy individuals.

Presentation with acute chest pain has previously been described in monilial esophagitis,[1] but it is unusual. Chronic, rather severe, dysphagia is more often the presenting symptom. Chronic dysphagia preceded the acute chest pain for months in our patient.

Diagnosis

This patient presented features not previously described. By Xray, esophageal moniliasis is usually reported to demonstrate a cobblestone irregularity of the lower 2/3 of the esophagus.[7] Other descriptions include a shaggy outline, ulceration, "shoulder" defects and segmental narrowing.[8] The apparent fistulae and the long and extensive luminal encroachment observed in our case, have not previously been described.

Endoscopically the exudate had a typical appearance but a mass lesion obstructing the esophageal lumen has not previously been reported.

Pathologic Nature of the Lesions

Opinions differ as to whether the roentgenologic irregularity represents mucosal edema, ulceration, colonies of monilia or pseudomembranes.[7] We saw breaks into the lesions simulating fistulae and a mass obstructing the esophagus. Biopsy of the mucosa failed to reveal organisms. These findings coupled with the dramatic disappearance of the lesions, indicate exophytic masses with pseudofistulae. The likely composition of these masses is monilial hyphae and exudate.

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University of Minnesota
Medical Alumni Meeting

The tentative program is as follows:

Friday, October 8, 1976

Alumni Luncheon—Radisson South
Speaker—Dr. Franz Hallberg, M.D.
Topic—Chronobiology

2:00 Scientific Seminar
Presented by 25th Alumni Class
Drs. Richard Lillehei and Byron Roberts, Co-chairmen

6:30-8:00 Social Hour
Radisson South, Poolside—cash bar

8:00 Annual Alumni Banquet—Radisson South
Presentation of Diehl Awards
Address—Dr. Peter G. Magrath, President, Univ. of Minn.

Saturday, October 9, 1976

10:00 Tour of new facilities
School of Health Sciences, Univ. of Minnesota

11:00-1:00 Chuckwagon Lunch
Owre, Millard and Jackson Hall quadrangle
Univ. of Minnesota on Washington Avenue

1:30 Homecoming football game
Minnesota versus Illinois

Contact: Minnesota Alumni Office, 2610 University Avenue, St. Paul, MN 55114.

The Calorie Intake of Patients with Advanced Cancer

ATHANASIOS THEOLOGIDES, M.D., Ph.D.;* JOY EHLERT, R.D.†
and B. J. KENNEDY, M.D.‡

Very limited data are available on the changes in food intake and meal patterns accompanying the appearance and the progression of cancer. The food intake of 39 cancer patients was evaluated: (1) prior to diagnosis, (2) at diagnosis, (3) on dissemination, and (4) on hospitalization for chemotherapy. At period 3, six patients complained of anorexia, 18 patients had a greater than 10% weight loss, and 14 patients had a greater than 300 Calorie drop in their daily intake. The decreased caloric intake was proportional for carbohydrates, protein and fat.

ANOREXIA WITH AN aversion to food are common manifestations of cancer. The resulting oligophagia contributes to progressive wasting and cachexia.[1,2] Although this oligophagia is a common finding in patients with cancer, there are no comprehensive studies available on the qualitative and quantitative changes in calorie intake with the progression of cancer from the early to the advanced stages.

To study such changes the food intake of patients with cancer was evaluated at four time periods: (1) Prior to the diagnosis of cancer. (2) At the time of the diagnosis. (3) At the time of the dissemination of the disease and (4) During the first hospitalization for chemotherapy or radiotherapy.

The calorie intake at these periods was compared between a group of patients having weight loss and another group without weight loss.

Patients and Methods

The study covered an eight-month period and involved patients admitted to the Medical Oncology Service of the Masonic Memorial Cancer Hospital of the University of Minnesota Medical Center. Patients included in the study met the following criteria: It was their first admission to our institution. The original diagnosis of cancer was made within three years prior to their admission. This period was selected arbitrarily for the patients to be able to make a rather accurate recollection of food intake prior to the diagnosis. During the previous three years, the patient should not have followed any medically or otherwise prescribed or self-imposed diet. During the hospitalization they should have been on a normal diet.

Patients were not included or were later excluded if they showed clinical signs of: (1) Edema and malignant intracavitary effusions, (2) Diarrhea, (3) Malabsorption, (4) Gastrointestinal obstruction, and (5) Obvious mental or emotional depression causing anorexia. Some patients were excluded also because they were discharged prior to completion of the study. Patients with any type of advanced cancer were accepted who had received no chemotherapy and radiotherapy.

Four hundred and thirty-nine patients were admitted to the Medical Oncology Service during the period of study. Sixty-eight were initially interviewed and 39 met the criteria and were eval-

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See editorial, page 553.

uated.

The questionnaire for the dietary recall recorded nutritional information for the first three periods. Period one represented the average daily dietary intake from six months to one year prior to the original diagnosis of cancer; period two, the average intake at the time of the diagnosis; and period three, the average dietary intake immediately prior to the admission during which this study was done. Except for the patients with chronic leukemia, period three actually represented the time of recurrence or dissemination of the cancer and admission for chemotherapy or radiotherapy. For period four, the caloric intake and distribution in the hospital was recorded for a minimum of three and a maximum of five days prior to chemotherapy or radiotherapy.

All dietary recalls and intakes were recorded on a standard hospital quantitative diet form. The intake in the hospital was calculated according to the diabetic exchange system of the American Dietetic Association for evaluation of carbohydrates, protein, fat and total caloric intake. The eating habits and the caloric distribution in the three main meals and any snacks between meals were also recorded.

The questionnaire included querries on the frequency and any changes in smoking and alcoholic beverage intake, and on any medications or other treatments received during the first three study periods. Changes in appetite, food cravings or food intolerances, aversions, and weight changes were recorded. Period one was used as a baseline for all patients. The intake in that period was compared to the 1965-1966 national survey of food and nutrient intake of individuals to determine whether there was any significant difference between the United States population as a whole and the patients studied. The caloric intake and the distribution of carbohydrates, protein and fat of every patient was compared to controls of the same age and sex from the national survey records.[3]

All 39 patients were initially analyzed as one group. The patients then were arbitrarily divided into two groups; group A included patients who from period one to period three had a weight loss of greater than 10% of their usual weight and group B patients with less than 10% loss or weight gain.

The diagnosis of the 39 patients included: carcinoma of the ovary—three, pancreas—one, rectum—two, colon—one, lung—six, breast—two, kidney—one, prostate gland—one, Hodgkin's disease—one, non-Hodgkin's lymphoma—10, osteosarcoma—three, melanoma—two, metastatic cancer from an undetermined primary—one, chronic myelocytic leukemia—two, and chronic lymphocytic leukemia—three. All patients had advanced disease at the time of admission.

Results

In period one, prior to diagnosis, the calorie intake of all 39 patients was comparable to controls from the National Survey Records[3] and within the limits or more than the recommended dietary allowances by the Food and Nutrition Board of the National Academy of Sciences for men and women of the same ages.[4] These allowances are designed for the maintenance of good nutrition of healthy people.

There were eighteen patients in the weight loss group A (six males and 12 females), with a median age of 62, mean 55 (range 16-81), and twenty-one patients (12 males and nine females) with a median age of 52, mean 53 (range 20-79) in the non-weight loss group B. The median period from diagnosis of cancer to the admission to the Medical Oncology Service was comparable in the two groups: 46 days for group A and 60 days for group B. The distribution of the various cancers was comparable in the two groups except for non-Hodgkin's lymphoma with two patients in group A and eight in group B.

Five patients in group A and one patient in group B stated that their appetite had decreased from period 1 to period 3. The remaining patients denied any anorexia prior to their hospitalization.

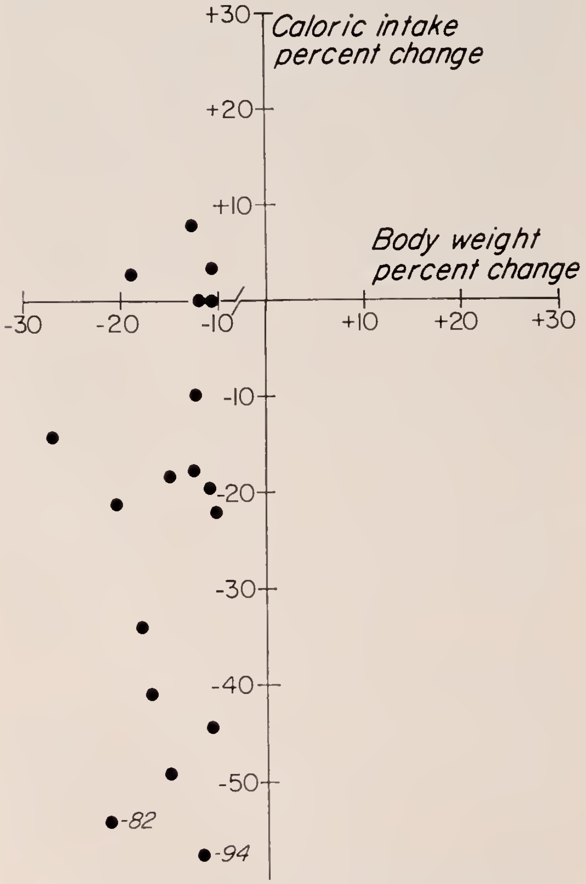
Of the 18 patients with weight loss (group A) six had a more than 300 calorie decrease of caloric intake from period 1 to period 2 (range 363-2,037) and 10 a decrease from period 1 to period 3 (range 301-2,241). Five of these 10 reported that their appetite was "still good" but the decreased intake was due to "easy filling."

Of the 21 patients without weight loss (group B) only one had greater than 300 calories decreased intake from period 1 to period 2 and four from period 1 to period 3 (range 453-1,315). The only patient with the anorexia in this group had the 1315 calorie decrease in the intake.

After admission to the hospital six patients in group A increased their calorie intake by more than 300 calories, six decreased it and the remaining six had no change. In group B, five had an increase, six a decrease and the remaining maintained the same calorie intake.

The decrease in caloric intake in the majority of patients in both groups resulted from a decrease in the three nutrients evaluated; carbohydrates, protein and fat. Occasionally, however, there were discrepancies such as increased consumption of one nutrient and decreased consumption of others. Various combinations were observed with no particular trend.

In group A the greater the calorie intake drop, the greater was the weight loss, but there were a few exceptions (Figure). The time lapse from period 2 to period 3 was, of course, important. For example, two patients had weight losses of 22.2 and 16.8 kg and had decreases of 300 to 570 calories in their intake from period 1 to period 3 respectively. However, the interval from the diagnosis and resection of the primary lesion (period 2) to hospital admission with disseminated disease was 326 days for the first patient with a carcinoma of the rectum and 107 days for the second patient with a carcinoma of the colon.



Figure—Correlation of weight change to caloric intake change in patients with more than 10% weight loss from period 1 to 3.

Patients with decreased caloric intake surprisingly retained their food preferences and meal patterns from period 1 to 3. The distribution of calories throughout the day remained unchanged. If the largest meal was at noon or in the evening it remained the most important meal even after the development of anorexia. No significant changes or any particular trends were observed in alcoholic beverage intake, in smoking habits, in food cravings and intolerances. Only increased coffee consumption after the diagnosis of cancer was mentioned by a few patients.

Discussion

Anorexia can be an early manifestation of cancer or can appear as the disease progresses.

Six out of 39 patients (15·3%) complained of anorexia on admission. This is higher than the 8.4% in males and 11.6% in females reported by Hoffman.[5] Ten more patients denied anorexia but complained of "easy filling" or early satiety despite a good initial appetite. This early satiety symptom is difficult to define but it is seen with increasing frequency as the cancer advances and especially after the institution of chemotherapy.

Our data on calorie intake for periods 1 to 3 depended on the patient's recollection of the intake relying entirely on memory. In many cases confirmatory information was obtained from relatives. However, it is appreciated that these data are of relative value. Especially when the changes in caloric intake were gradual the patient might not have appreciated the magnitude of the changes and underestimated the intake before the diagnosis.

In general it was observed that there was correlation between the calorie intake drop and the weight loss. However, there were exceptions in both directions: patients with unchanged intake and weight loss and patients with decreased intake and stable weight. The latter has been attributed to increased total body water in patients with advanced cancer.[1]

A few patients without anorexia and with a calorie intake within the national average for their weight, age, and sex and within the recommended allowances for maintenance of good nutrition in healthy persons had significant weight loss. Intestinal malabsorption, increased metabolism and energy expenditure and other factors might have contributed to this phenomenon.[1,7-9]

Limited data are available in the literature on the calorie intake of patients with cancer.[5] These data too based on recollection have the same pitfalls as noted here. Furthermore they represent intake changes at the time of diagnosis of cancer without data on further changes during the course of the disease.

Intake data collected while the patient is in the hospital are more objective. However, the hospital food with limited selection might contribute to oligophagia. Analgesics, sedatives and other medications might also aggravate the anorexia.

Despite the anorexia and the oligophagia the calorie distribution throughout the day and the meal patterns remained unchanged and no particular aversions to meat or any other food was noted. This was surprising because of the common belief that breakfast is the major meal of the cancer patient and that the anorexia and early satiety become worse as the day progresses.

Prospective studies are needed to correlate the anorexia, oligophagia, and weight loss to type and location of cancer, to chemotherapy, to regression and to progression of the disease. The role of nutritional rehabilitation in clinical improvement, treatment tolerance and prolongation of survival also needs extensive study.

Summary

Anorexia and oligophagia are common manifestations of cancer. The food intake of cancer patients was studied at four periods: prior to diagnosis, at diagnosis, at the time of dissemination of the disease, and during first hospitalization for chemotherapy or radiotherapy.

Thirty-nine patients with various cancers were evaluated. Eighteen had weight loss greater than 10% of their usual weight, and 21 had less or no weight loss on admission. Five of the 18 and one of the 21 had anorexia. Ten of the 18 and four of the 21 had greater than 300 calories decrease in their daily food intake. The decrease was usually in all three nutrients. There was a correlation between oligophagia and wasting but weight loss with unchanged caloric intake and stable weight with decreased intake were also observed. Patients with decreased intake maintained their food preferences and meal patterns. No food cravings or intolerances were observed.

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Medical Alumni of Hennepin County Medical Center

A reunion of all medical alumni of Hennepin County Medical Center (Minneapolis General Hospital, Hennepin County General Hospital) will be held in Minneapolis October 14, 15 and 16, 1976. For information, write to Eldon Berglund, M.D., Hennepin County Medical Center, Minneapolis, Minnesota 55415.

Letters to the Editor

We would like to encourage physicians to contribute to the Letters to the Editor Section. We want to hear what you have to say, what you think, why you hold certain opinions. In short, we want to make this as lively and spirited a section as possible.

The Editors

Current Status of the Radioactive ^{131}I Uptake Test

Effects of Gelatin Capsules and Dietary Iodine

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There was no difference in the uptake of radioactive ^{131}I by the thyroid of subjects administered ^{131}I orally in gelatin capsule and liquid form. The uptake of ^{131}I by the thyroid 24 hours after oral administration (U_{24}) was significantly reduced in our subjects when compared to normal measurements of 10 to 15 years ago. Elevated urinary excretion of iodine by subjects and alterations of iodine kinetic studies suggest a relatively high intake of dietary iodine. Chemical analysis of hospital and nursing home diets revealed high iodine content. However, drinking water, commercial bread, milk, and a widely used emulsifying agent did not contain large amounts of iodine. Physiologic adaptation ("autoregulation") lowers thyroid uptake during periods of high iodine intake. Although the U_{24} remains a useful adjunct for the diagnosis of Grave's disease, the test is no longer suitable for the diagnosis of hypothyroidism. Diminished thyroid uptake may also interfere with ^{131}I therapy for thyroid cancer and hyperthyroidism and increased dietary iodide may diminish the remission rate of hyperthyroidism after antithyroid drug treatment. Current levels of dietary iodine are safe, but further increases may result in thyroid dysfunction in predisposed patients.

A SUBSTANTIAL DECREASE IN the thyroid uptake of radioactive ^{131}I has occurred over the past 10 to 15 years.[1-14] Halpern and coworkers[15] postulate that gelatin capsules, introduced as a vehicle for ^{131}I, interfere with the absorption of the isotope thus lowering thyroid uptake. Most authorities, however, attribute the lowering of thyroid uptake to an increased intake of dietary iodine.[3,11,16] Changing food habits, agricultural practices, and techniques of food processing and marketing suggest that greater amounts of iodine are now consumed in the United States from bread, dairy products, food additives, and other sources.[17,18]

We report the thyroid uptake of ^{131}I administered in capsule and liquid form and the iodine content of drinking water, bread, milk, a widely used emulsifying agent, and hospital and nursing home diets in the LaCrosse, Wisconsin area. We also review the kinetics of iodine metabolism, discuss the effects of increased iodine intake on thyroid function, reassess the role of thyroid uptake studies in the diagnosis of thyroid disorders, and consider that increased dietary iodine may produce thyroid dysfunction.

Materials and Methods

We measured the uptake of ^{131}I by the thyroid one (U_1), four (U_4), and twenty-four hour (U_{24}) after the oral administration of ^{131}I in nine healthy volunteers. These subjects were clinically euthyroid, had a normal free thyroxine equivalent (FTE), were taking no iodine-containing medications, and were ingesting a normal diet. Five subjects received 25 to 30 μCi of ^{131}I in gelatin capsule form, and the other four received an aqueous solution of ^{131}I (available from Mallinckrodt Nuclear, St. Louis, Missouri). Three to four weeks later, the studies were repeated and the subjects were administered the other form of ^{131}I. The urinary excretion of iodide (E) was estimated by the creatinine index method[19] in all subjects.

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We purchased various brands of bread and milk from local grocery stores in 1973 and 1974. A slice from each loaf of bread was dehydrated at room temperature for 24 to 48 hours in a desiccator. Nine meals from the general menu of La-Crosse Lutheran Hospital (breakfast, lunch, and supper) for three days were homogenized without added salt in a Waring blender. Four meals (breakfast, two lunches, and one supper) from an area Nursing Home were similarly blenderized. Twenty-four hour urine collections from six elderly but healthy residents from the Nursing Home were collected; none of the residents were receiving iodine-containing drugs. An aliquot of a commonly used emulsifying agent, Carostay Type S,® was obtained from Stauffer Chemical Company, New York, New York 10017. Liquid specimens including drinking water were frozen and aliquots from all specimens were analyzed for iodine by the Mayo Clinic Laboratories.*

Results

The means of thyroid uptakes determined one, four, and 24 hours after the oral administration of ^{131}I in gelatin capsule form (Table 1) were not significantly different from the means of thyroid uptakes determined after the oral administration of aqueous ^{131}I.

Drinking water contained 12 μg of iodine per liter.

The iodine content of various brands of bread (Table 2) ranged from 0.7 to 26.7 μg per slice in 1973 and 0.2 and 12 μg per slice in 1974. Five brands of milk contained from 2.4, 5.0, 5.5, 2.4, and 41.5 μg per 250 ml serving, respectively. The iodine content of Carostay Type S® was 136 μg per gram.

TABLE 2
Iodine Content of Local Bread

1973 Brand	1973 μg./slice	1974 Brand	1974 μg./slice
A	26.7	A	12
B	13.2	B	0.5
C	0.9		
D	0.7	J	0.6
E	14.5, 3.7	K	2.1
F	24.3	L	0.8
G	4.1	M	0.2
H	3.3	N	0.9
I	1.3	O	1.0

The iodine content of the general diet from La-Crosse Lutheran Hospital (Table 3) ranged from 83 to 158 μg for breakfast, 94 to 152 μg for lunch, and 49 to 196 μg for supper. Total daily dietary iodine ranged from 246 to 506 μg. The iodine content of meals from the general menu of the Nursing Home (Table 3) was higher; total dietary iodine for one day was 1531 μg.

TABLE 3
Iodine Content (μg) of Blenderized Diets
La Crosse Lutheran Hospital

Day	Breakfast	Lunch	Supper	Total
1	83	114	49	246
2	112	94	173	379
3	158	152	196	506
Mean	117	120	139	377
		Nursing Home		
	596	708 91	227	1531

The urinary excretion of iodine in nine healthy control subjects (Table 1) ranged from 205 to 1,125 μg per 24 hours (mean 514 ± 284 μg)

TABLE 1
Thyroidal Uptake of Radioiodide ^{131}I: Capsule vs. Liquid

Subject	E	Capsule U_1	Liquid U_1	Capsule U_4	Liquid U_4	Capsule U_{24}	Liquid U_{24}
	μg./24hr. (351 ± 45)*	% (2.8 ± 1.3)*		% (6 ± 3)*		% (12.1 ± 6.1)*	
L.J.	315	2.8	0.9	4.4	3.0	8.5	8.7
M.S.	301	1.1	1.6	1.3	4.1	4.8	9.8
A.B.	254	2.7	3.5	6.9	4.8	15.7	8.2
J.Z.	435	0.4	3.0	3.1	1.2	10.6	4.9
L.J.	1125	2.2	1.4	4.8	1.3	5.8	2.7
O.H.	806	2.2	3.7	4.8	4.9	5.6	8.6
V.F.	611	1.6	2.2	4.8	3.1	9.1	8.2
S.B.	576	2.1	1.7	5.7	3.3	13.0	10.3
V.B.	205	3.1	2.7	7.3	4.2	14.6	6.9
Mean ± s.d	514 ± 284	2.0 ± 0.9	2.3 ± 1.0	4.6 ± 1.9	3.3 ± 1.4	9.7 ± 4	7.6 ± 2.4

*Results obtained in 1971 in 44 euthyroid subjects[7] and in six healthy nursing home residents from 421 to 956 μg per 24 hours (mean 656 ± 231 μg).

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*Iodine determinations of drinking water and Carostay Type S® were performed by Bioscience Laboratories, Van Nuys, California.

Discussion

Our study indicates that thyroid uptake of ^{131}I is not affected by the use of the Mallinckrodt gelatin capsules. Halpern and coworkers[15] noted a delay in the onset and a decrease in the thyroid uptake at 24 hours when ^{131}I was administered in a gelatin capsule (Squibb) rather than in liquid form. They postulated that the differences were due to reactions involving the gelatin capsule. Robertson and coworkers[14] studied thyroid uptake of ^{131}I in capsule form obtained from two commercial sources (Squibb and Mallinckrodt Nuclear) and in aqueous form (Squibb) and noted a decrease in uptake with the Squibb capsule, which contains Gelfoam as a filler. Because Gelfoam is dissolved slowly by 1N HCL, the authors postulate that failure of the Gelfoam-filled capsule to dissolve in the stomach may be responsible for the delay of ^{131}I uptake. No decreases were noted in four patients studied with the Mallinckrodt capsules, which have sodium phosphate as a filler.

The uptakes at one, four, and 24 hours (Table 1) are similar to results obtained in our laboratory in 1971[7] when we obtained values of 2.8 ± 1.3%, 6.0 ± 3%, and 12.1 ± 6.1%, respectively in 44 euthyroid subjects who were tested with gelatin capsules (Abbott Laboratories, North Chicago, Illinois) dissolved in water. The data obtained in both studies are significantly lower than results previously considered normal.[20] Diminished U_{24} has also been noted in many parts of the country.[1-14] Studies performed in the same laboratory several years apart indicate that the decrease in U_{24} has occurred in the last 10 to 15 years.[3,5,6,12]

Iodized salt has been widely utilized in this country for over forty years. A recent survey[21] indicates that although sales of iodized salt has increased to 54.8% of the total, the nationwide per capita consumption of all salt decreased from 4.42 g per day in 1959 to 3.42 g per day in 1968. Thus the average intake of iodine from iodized salt is 260 μg per day. Although fish and fish products contain relatively high concentration of iodine, seafoods are not a major dietary item in the United States. The iodine content of LaCrosse drinking water is 12 μg per liter. Thus iodized salt, seafood, and drinking water are unlikely sources of increased dietary iodine.

In 1955, a continuous—mix process for the manufacture of commercial bread was introduced. This process utilizes a number of ingredients that contain iodine to "stabilize" the bread. A very high iodine content of commercial bread was first noted in 1965.[17] Pittman and coworkers[3] confirmed this finding and reported that a single slice of commercial bread contained up to 160 μg per slice. It has been assumed that bread is a major source of the apparent increase in dietary iodine. However, the iodine content of several commonly used commercial breads purchased in LaCrosse, Wisconsin in 1973 and 1974 is low. This is in agreement with a study from New York City[6] in which the iodine content of six randomly selected brands of commercial bread ranged from 0.3 to 32.4 μg per slice, most samples having less than 6 μg per slice. In another study,[11] the iodine content of unpackaged Jewish breads commonly eaten in Bronx, New York, ranged from undetectable amounts to 9.5 μg per slice. Commercial bread from Columbus, Missouri had iodine contents ranging from undetectable amounts to 269 μg per slice. Recent surveys,[18] suggest that other "stabilizers" may be replacing iodine-containing dough conditioners.

Milk from dairies in LaCrosse contained from 2.4 to 41.5 μg per 250 ml serving. Hemken et al.[22] reported milk iodine values from 13 Illinois farms averaged 425 μg per liter, and samples from eight Maryland farms averaged 457 μg per liter. The range in iodine content of milk was wide and reflected the level of iodine supplementation more than the iodine content of hay, silage, or grain.

The widespread use of sanitizing agents such as iodophors in the dairy industry may be an indirect source of iodine in the human diet. Iwarsson and Ekman[23] have shown that during periods of teat dipping, the iodine content of milk increased 174 μg per liter (range 55-353 μg per liter) in comparison to periods when no iodine disinfectants were used. In Tasmania, milk from five localities where iodophors were used as sanitizing agents contained 113-346 μg of iodine per liter; milk from dairies in the same localities not using iodophors contained only 13-23 μg per liter of iodine.[24] Thus the iodine content of bread and milk may vary between communities depending on local baking or agricultural practices.

Alginates—widely used as emulsifiers, stabilizers and thickeners—are a potential source of dietary iodide. The iodide content of one such agent, Carostay Type S,® was 136 μg per gram. It has been estimated that the average iodine intake from alginates in the United States is less than 1 μg per day.[18]

Erythrosine®, is a dye liberally used in food and drugs. Studies with rats reveal that the erythrosine contained in commercial cereal is deiodinated and the liberated iodine elevates thyroidal and urinary iodide.[27] If erythrosine is deiodinated in a similar fashion in man, a single serving of erythrosine-containing cereal would contribute approximately 440 μg of iodide to the diet.

Food consumption patterns in the United States exhibit an increasing trend toward the use of commercially processed and prepared food. Although the use of iodized salt is minimal, recent reports suggest that processed and prepared food may contain high amounts of iodine from unidentified sources.[18] For instance, the iodine content of 12 types of frozen fried-chicken dinners ranged from 9.9-430 μg per package.[25] In another study,[26] the Wisconsin Alumni Research Foundation, Inc., analyzed the nutritive quality of the products of a franchised food corporation. The consumption of one meat-containing product, one serving of french fries, and a chocolate milk shake provided between 125 and 156% of the recommended daily allowance (150 μg per day) for a 14-18 year old male. The source of the iodine was not specified.

LaCrosse Lutheran Hospital meals (Table 3) contained from 246 to 506 μg per day and meals from the Nursing Home contained 1531 μg per day. Although only a limited number of investigators have measured total dietary iodine intake, several studies provide data that suggest total iodine intake is increasing. Vought and London[28] reported in 1964 the range in individual daily iodine content of 18 metabolic diets was 15 to 219 μg per day (mean 89 μg per day). Analysis of 36 individual meals (without added salt) indicated a daily range of iodine intake of 65 to 529 μg per day. In a subsequent study,[29] Vought and London measured dietary iodine intake in 13 healthy nonhospitalized subjects. Total iodine intakes ranged from a low of 18 μg per day by one adult female to a high of 1540 μg per day by an adolescent male. The range of mean daily iodine intake values were from 58 ± 7 to 830 ± 252 μg per person. Pittman et al.[3] report daily iodine content of the University of Alabama Hospital ranged from 274 to 842 μg per day (mean 533 ± 82 μg per day); the iodine content of the diet of the Birmingham Veteran's Administration Hospital ranged from 595 to 713 μg per day (mean 677 ± 19 μg per day).

As the kinds and sources of food become more diversified and the use of various iodine-containing food additives becomes more widespread, the amount of iodine consumed per meal and per day will become more variable. This is illustrated by the difference of the iodine content of lunch at the Nursing Home (91 and 708 μg) and the range of daily intake from 246 to 506 μg in the hospital diet. Although the source of dietary iodine has not been identified in this study, the current diet in LaCrosse and throughout the country generally is increasing in iodine content and exceeds amounts recognized for adequate nutrition.

An indirect estimate of dietary iodide intake can be obtained by measuring the daily urinary iodine excretion (E). The average excretion values of 514 ± 284 μg per 24 hours obtained in nine subjects (Table 1) and 656 ±231 μg per 24 hours determined in six healthy nursing home residents is higher than the mean excretion of 351 ± 45 μg per 24 hours obtained in 44 euthyroid subjects in 1971 (Figure 1). Pittman et al.[3] reported average daily excretion values of 640 ± 70 μg per 24 hours in Central Alabama. Urinary excretion of iodine ranging from 100 to 467 μg per 24 hours[14] reported from Rochester, Minnesota, is also higher than the mean value of 150 μg per 24 hours usually reported as normal (cf. review by De Groot[30]).

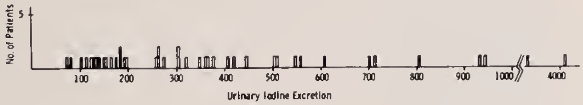

Fig. 1—Distribution of urinary iodide excretion in 44 euthyroid subjects.

We assessed several indices of iodine kinetics in 44 healthy subjects.[7] In addition to the increased E, the mean plasma inorganic iodide (PII) of 0.79 μg per 100 ml is higher and the clearance of iodide by the thyroid gland (C_G) of

5.9 ml per min is lower than values cited in the literature.[20,30] The normal renal clearance of iodide (C_K) indicates that the elevated PII and E are due to increased intake of iodine rather than from an abnormality of renal function. The low U_{24} values are the result of normal autoregulatory mechanisms that occur during periods of high iodine ingestion.[31] The low C_G partially compensates for the high PII. In addition, the rapid release of non-hormonal iodine from the thyroid gland provides a second mechanism for maintaining normal thyroid hormone economy during periods of relatively high iodine ingestion.

We reviewed the U_{24} measurements performed for diagnostic purposes in 12 hypothyroid, 45 hyperthyroid, and 65 euthyroid patients.[32] Of the hyperthyroid patients, 36 had Graves' disease while the remaining nine had toxic nodular goiter (TNG). The mean and standard deviation of euthyroid, hypothyroid Graves' disease, and TNG patients were 14.3 ± 7%, 3.9 ± 3%, 52.9 ± 18.4%, and 25.2 ± 10.3%, respectively (Figure 2). Because of the marked overlap between the U_{24} of the euthyroid and hypothyroid patients, this test is unsuitable for the diagnosis of hypothyroidism. Patients with TNG also may have U_{24} within the normal range. Patients with hyperthyroidism owing to Graves' disease are usually easily differentiated from euthyroid patients. However, one of our patients with well established Graves' disease had a very low U_{24} (Figure 2). The patient was not receiving iodine-containing medications. Patients with Graves' disease and chronic thyroiditis are sensitive to iodine; as little as 2 mg of a saturated solution of potassium iodide (SSKI) daily will markedly suppress the U_{24}.[33] Because urinary excretion of iodine exceeds 2 mg in some of our subjects, dietary iodide may suppress the U_{24} and obscure the diagnosis of hyperthyroidism.

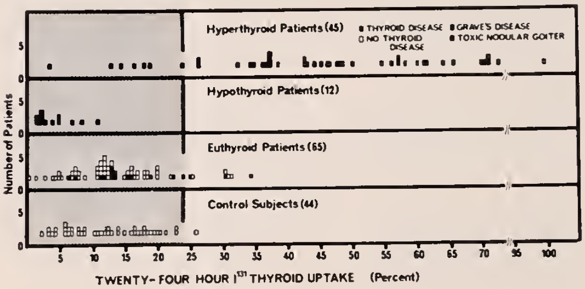

Fig. 2—Distribution of 24-hour thyroid uptake in control subjects, euthyroid, hypothyroid, and hyperthyroid patients: The shaded area represents the normal range established by using the mean ± two standard deviations of the control subjects. (Reproduced from Caplan et al.,[32] Internal Medical Digest 8:34-42, 1973, with permission of the publishers.)

Despite the diagnostic limitation of the U_{24}, there remain certain indications for this test including: (1) in the diagnosis of Graves' disease where other data are inconclusive, (2) to calculate the dose of radioiodine for treatment of hyperthyroidism, (3) as an integral part of thyroid suppression, stimulation, and perchlorate washout tests; and (4) in the evaluation of enzyme abnormalities resulting in defects of thyroid hormone synthesis.

Increased dietary iodide may interfere with the treatment of thyroid disorders. For instance, radioactive ^{131}I cannot be used for the treatment of hyperthyroidism in patients with very low thyroid uptakes. For this reason, the U_{24} should be performed in all patients prior to the administration of a therapeutic dose of radioactive iodine. Furthermore, since the lowering of the U_{24} may require the administration of larger doses of radioactive iodine, it appears desirable to utilize the U_{24} for calculating the therapeutic dose.

Fifty to 75 mCi of ^{131}I is the usual dose used to ablate a thyroid remnant after surgery for thyroid cancer. We have three patients in whom this dose was insufficient to destroy the remnant. Because the decreased uptake of ^{131}I may be due to increased dietary iodide, it might be desirable to deplete body stores of iodine prior to ^{131}I treatment for thyroid cancer, thus allowing greater uptake of the isotope by the functioning cancer.[34]

Permanent remissions are expected in approximately 50% of patients with Graves' disease treated for a year with thionamide antithyroid drugs. A recent study, however, reports a remission rate of only 13.6%.[35] In another study,[36] the addition of 200 μg of potassium iodide during or after antithyroid drug treatment in patients with Graves' disease significantly decreased the remission rate. Thus, increased dietary iodide may reduce permanent remissions in hyperthyroid patients treated with antithyroid drugs.

The inhibitory effect of large amounts of iodine on thyroid hormone synthesis and particularly secretion account for its beneficial effects in the treatment of hyperthyroidism. The normal thyroid gland is insensitive to the inhibitory effects of iodine since it has the ability to prevent intracellular iodine accumulation necessary for these anti-thyroid effects.[31] In patients with a thyroid dysfunction, however, this adaptation ("autoregulation") does not occur. Thus, high intracellular iodine concentrations are maintained when the iodine intake is pharmacologically increased. Consequently, goiter and hypothyroidism can be produced in such patients.[37-,38] In the recent Ten-State Nutritional Survey (cf. Kidd et al.,[39] goiter prevalence was higher among persons excreting high levels of urinary iodine (>799 μg per gram creatinine). However, the goiters were small and there was no clinical or biochemical evidence of thyroid dysfunction.

Iodine administration induces hyperthyroidism in subjects residing in endemic goiter areas.[40] This phenomenon, termed "Jodbasedow," has again been noted when potassium iodate was added to bread throughout Tasmania in 1966 for prophylaxis against endemic goiter.[41] Daily intake of iodine from bread ranged from 80 to 200 μg. The development of hyperthyroidism in patients with autonomously functioning thyroid nodules has also been produced by the administration of as little as 500 μg of SSKI daily.[42] Until recently, this phenomenon was thought to be limited to endemic goiter areas. Vagenakis and coworkers,[43] however, described the development in hyperthyroidism after administration of SSKI in large doses to a group of patients with sporadic, nontoxic nodular goiters in Boston. Cases of hyperthyroidism following the administration of radiographic contrast media that contain iodine have also been reported.[44]

Although there are some suggestions that relatively high iodine intake may be associated with the development of goiter,[37] it is not possible to define specific adverse effects on health associated with moderately high iodine intake.[39] To date, hypo- and hyperthyroidism have been precipitated only by pharmacologic doses of iodine and the current iodine content of foods is not thought to be a health hazard.[45] However, if iodide intake continues to increase, hypo- and hyperthyroidism may develop in predisposed individuals.

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Northwestern Pediatric Society
Annual Meeting—September 17, 1976

The annual meeting of the Northwestern Pediatric Society will be held Friday, September 17, 1976 at the Chanhassen Dinner Theater, Chanhassen, Minnesota.

Original papers will be presented and the guest speaker for the occasion will be Charles L. Scriver, M.D., geneticist with the McGill University and Montreal Children's Hospital. Dr. Scriver's subject will be "Genetics: A Voyage to Discovery."

Contact: Ray C. Hippchen, M.D., Secretary-Treasurer, 730 E. County Road B., St. Paul, Minnesota 55117.

The Spectrum of Agricultural Medicine

RICHARD W. RASMUSSEN, M.D.[*] and GEORGE A. COLE, M.D.[†]

The agricultural worker is exposed to many disease processes that are unique to his occupation. These processes—accidents, infectious diseases, chemical toxicity, respiratory conditions, and environmental exposures—are reviewed according to their etiologies. An awareness of these problems will allow the physician to deal more effectively with them.

In 1972, 9,610,000 Americans (4.6% of the population) were engaged in agricultural work on 2,730,250 farms.[1] This large group of people is exposed to many disease processes that are unique to their occupation. Physicians and other health professionals involved in the care of patients with a rural background should maintain a constant awareness of these diseases.

There are five major kinds of problems in agricultural medicine (Table).

TABLE
Five Major Problems in Agricultural Medicine

1. Farm accidents
2. Infectious diseases
3. Chemical toxicity
4. Respiratory conditions
5. Environmental exposure

Farm Accidents

Of occupation-related deaths in the United States, farm accidents are second only to those in construction industries.[2] In 1973, 6,300 farm residents lost their lives in accidents (61 per 100,000 farmers) and another 560,000 suffered disabling injuries.[2]

Accidents involving farm machinery accounted for 29% of work-related injuries. The tractor was involved in 40% of these accidents (8.6 deaths per 100,000 tractors).[2] The major modes of injury include: turning over on rough terrain, being run over by one's own tractor after failing to disengage the engine, and power take-off injuries. Wagons, harvesters, corn pickers, and conveyor accidents accounted for the remainder. These injuries are often related to attempting to service the equipment while it is still running and to removing safety features.[3]

Falls from barns, tractors, and ladders were the leading cause of farm accidents, accounting for one-third. Other types of injuries included collisions with moving or falling objects or animals, burns, and lifting accidents.[2]

There are multiple causes of farm accidents. Fatigue, the pressure of working against deadlines in all types of weather, inexperience, underlying illness, and poor equipment all have been implicated as possible causative factors, but carelessness appears to be the predominant one.[3]

Infectious Diseases

The close and continuing association between the farmer and his livestock and land predisposes him to certain infectious processes. Public health surveillance and inspection programs have greatly reduced the incidence of many of the zoonoses but have not eradicated them as a cause of disease in the agricultural population.

With the exception of salmonellosis, the bacterial zoonoses affecting man are relatively infrequent (only 589 cases in 1974).[4] Three of the bacterial zoonoses, anthrax, bovine tuberculosis, and glanders, essentially have been eradicated from the United States, although they continue to be present in underdeveloped countries.

Brucellosis, tularemia, and tetanus still are endemic in agricultural communities throughout the world. In fact, 197 cases of brucellosis occurred in the United States in 1974.[4] Brucellosis should be suspected in any hog or cattle farmer with fever of insidious onset, headache, anorexia, and generalized malaise.[5] Exposure to the infection frequently occurs during removal of a bovine placenta. The presence of an ulcerated skin lesion and tender, fluctuant, regional lymph nodes should arouse suspicions of tularemia, particularly if there is a history of contact with wild rabbits.[6] *Clostridium tetani* is commonly found in the superficial layers of the soil; hence farmers are more vulnerable to infection. The disease is preventable by active immunization of all agricultural workers and their families.

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See editorial, page 552.

Psittacosis or ornithosis is generally felt to be a disease of parrot and parakeet handlers but has occurred in epidemics in farmers and poultry producers working with turkeys and ducks.[7]

Salmonellosis continues to be an immense public health problem today. It is the most common disease transmitted from animal to man and is often isolated from chickens, turkeys, ducks, pigs, and cows.[7] The farmer is continuously exposed to these animals and their excretions.

The agricultural worker is vulnerable to several viral diseases transmitted from animals. Rabies in man has become a rare disease, but a continuous awareness must be maintained due to the virtually uncontrollable sylvatic population. People in rural areas are at greater risk because of their proximity to fox and skunk populations. Newcastle disease may be transmitted to man and may cause conjunctivitis.[8] Cowpox and pseudocowpox may occur following contact with infected cattle. Orf, or ecthyma infectiosum, presents as a papule that enlarges to form a hemorrhagic bullous lesion that later ulcerates. It occurs following cutaneous contact with the infected mouth sores of sheep.[9]

Histoplasmosis, blastomycosis, sporotrichosis, and coccidioidomycosis occur in people who work with soil and plants. Histoplasmosis and blastomycosis may cause illnesses varying from mild influenzalike syndromes to chronic pulmonary or disseminated disease.

Histoplasmosis results from inhalation of fungus-containing dust contaminated by bird or bat dung. Human disease may result from exposure in chicken houses or pigeon cages, during exploration of bat-infested caves or buildings, or during cleanup of starling nesting areas. Outbreaks of acute pulmonary histoplasmosis complicated by erythema nodosum and erythema multiforme occurred in Mason City, Iowa, in 1962 and 1964 after attempts to clean trees and underbrush from a starling roosting area in the center of town.[10]

An interesting epidemic of acute pulmonary blastomycosis occurred in the town of Big Fork, Minnesota, in 1972 when members of four families worked on the construction of a small cabin in a wooded area.[11]

Sporotrichosis is a truly occupational fungal disease that usually causes cutaneous and contiguous lymphatic infection after local implantation in the skin. Disseminated sporotrichosis from inhalation infection of the lungs is rare. The usual clinical picture of the cutaneous lymphatic form of the disease is one of a papule, nodule, or pustule, generally located on the upper extremity, which may form an indolent ulcer. There is associated lymph node enlargement and possibly ulceration in the lymph chain draining the primary lesion. The fungus is found in saprophytic form in soil, peat moss, salt hay, and on thorns of rose and barberry bushes. Thus cutaneous disease may occur in farmers, gardeners, or florists after accidental skin inoculation with the organism.[12]

Rocky Mountain spotted fever and Q fever are occupational diseases of livestock workers and dairy farmers.

The only occupational spirochetal disease of agricultural workers is leptospirosis. This disease has protean manifestations, which may include fever, jaundice, renal failure, hemorrhagic manifestations, myocarditis, aseptic meningitis, characteristic conjunctival suffusion, and truncal or pretibial rash. Multiple clinical syndromes may result from infections by a single leptospiral serotype or a single syndrome may be caused by different serotypes of the organism. Therefore, the general term "leptospirosis" has replaced the previous nomenclature of canicola fever and Weil's disease.[13] The animal hosts are both wild (rats, skunks, raccoons, and foxes) and domestic (pigs and cattle). Transmission to man is via direct contact with the urine or tissue of the infected animal or through contaminated soil or water.[14]

Parasites are not a common problem of the agricultural population of the United States. Cysticercosis is more common among people closely associated with hogs. *Echinococcus granulosus* infections have occurred in sheep ranchers in the central valley of California.[15] Amebiasis, both intestinal and hepatic, is unusual in the United States but still occurs as a result of poor sanitation with fecal contamination of food and water. Diarrhea and steatorrhea caused by infection with *Giardia lamblia* are occasionally encountered in rural areas with contaminated water sources.

Chemical Toxicity

Coincident with the growing world population is an ever-increasing demand on the agricultural sector of society to expand its production to meet world needs. The increased production has been largely due to the use of pesticides and fertilizers. These chemical agents are hazardous to the agricultural worker and his environment. As the dangers of the older pesticides (DDT) become recognized, newer agents are continuously released for use, but they too may be dangerous.

Chemicals used in the agricultural industry can be categorized according to their principal use: insecticides, rodenticides, fungicides, herbicides, fumigants, and fertilizers.

Some of the most toxic chemicals to which agricultural workers are exposed are insecticides. The chlorinated hydrocarbons (aldrin, DDT, dieldrin, endrin, heptachlor) may produce intoxication via inhalation, ingestion, or percutaneous absorption. The toxicity varies with the degree of exposure and the solvent in which the agent is dissolved. Initial symptoms include nausea, vomiting, headache, dizziness, and tremors that may progress to central nervous system hyperexcitability with convulsions.[16] Treatment is primarily supportive, and sedatives are used to control seizures. These chemicals are now restricted and may be used for only specific purposes defined by the United States Department of Agriculture.

The phosphate ester or organophosphate insecticides (parathion, malathion, and phorate) also carry significant toxicity to man through their irreversible inhibition of cholinesterase. After absorption through the skin, lungs, or gastrointestinal tract, they cause an accumulation of acetylcholine with diffuse parasympathetic stimulation. Clinical manifestations include miosis, blurred vision, abdominal cramps, diarrhea, vomiting, wheezing, bradycardia, weakness, convulsions and coma.[17] Treatment consists of induced emesis, catharsis, washing of the skin, atropine, and pralidoxime chloride. After chronic exposure, the patient may note forgetfulness, slow and incomplete mentation, visual disturbances, myalgia, and loss of interest in work.[18] The carbamates (carbofuran, carbaryl) produce a similar clinical picture secondary to inhibition of cholinesterase.

The older insecticides, lead, arsenate, arsenite, and nicotine, continue to be used but have largely been replaced by the newer agents.

The rodenticides (sodium fluoroacetate, strychnine, thallium sulfate, and warfarin) have been used for many years. They all carry significant toxicity. Thallium toxicity causes nervous system, hepatic, and renal damage as well as uniquely characteristic alopecia. The sale of this agent formerly used as an ant, roach, and rodent poison has been banned because of frequent human toxicity. However, some thallium-containing products still may be found in residual stocks in homes.

The commonly used fungicides of the dithiocarbamate group (maneb, zineb, and ferbam) are of relatively low toxicity to man. They may cause dermatitis, conjunctivitis, or upper respiratory irritation following contact. More toxic agents such as formaldehyde, phenol, and compounds of copper, mercury, tin, and zinc continue to be used.[19]

The herbicides or weed killers have been associated with relatively few adverse effects. The chief problem with propachlor (Ramrod), alachlor (Lasso), atrazine, and Treflan is contact dermatitis. The more toxic herbicides include maleic hydrazide which causes tremors and muscle spasm; sodium chlorate, which leads to methemoglobinemia and gastritis when ingested; and dinitrophenol, which may cause hyperthermia and death.[19]

Fumigants are volatile chemicals used in agriculture to control insects in stored grain or to fumigate barns. The halogenated hydrocarbons (carbon tetrachloride, ethylene dichloride, and ethylene oxide) are the major group employed. Their toxic effects, hepatic necrosis and a renal tubular necrosis-like picture, are well recognized.

Anhydrous ammonia is widely employed in agriculture as a fertilizer because of its 82% nitrogen content. During transport, storage, and application, it presents several hazards to the agricultural worker. Depending on the concentration and duration of exposure, it may produce respiratory tract damage varying from pharyngitis to bronchitis to pulmonary edema.[20] Ammonia will produce first and second degree burns of the skin by its freezing or alkaline actions. Contact with the eye may result in damage, ranging from conjunctivitis to corneal ulceration with secondary glaucoma. The mainstay of therapy is early copious irrigation of the exposed area with water.

Respiratory Conditions

Several respiratory conditions that are unique to agricultural workers have been described. They may be classified as secondary, direct chemical irritations or as allergic interstitial pneumonitis.

The first of the allergic processes to be described was farmer's lung. This disease is a hypersensitivity reaction to thermophilic actinomycetes that grow in moldy hay, corn, grain, or tobacco. Clinical symptoms include fulminant or insidious development of fever, cough, and dyspnea.[21] Treatment consists of removing the patient from the offending agent and instituting supportive respiratory care. The patient's serum usually contains precipitating antibodies to moldy hay extracts.

Mushroom-worker's lung is a similar disease that occurs following respiratory contact with the actinomycetes present in the mushroom beds of horse manure.

The occupational diseases bagassosis, byssinosis, and grain-dust-worker's lung are primarily found in mill and factory workers.

Several chemicals common to the agricultural environment have their primary effect on the lung. Many of the pesticides and fertilizers previously described can cause respiratory disease.

Since Hayhurst and Scott's description[22] in 1914, there have been several reports of patients experiencing respiratory distress or death after entering a silo. In 1956, nitrogen dioxide was identified as the toxic agent.[23] It is formed from plant nitrates during storage. Plant nitrate levels are increased by drought, fertilizers, and prolonged exposure to light. Nitrogen dioxide is produced between 18 hours and 10 days after storage.[24] The clinical picture is that of a farmer who, after exposure to a yellow-brown gas in the lower part of a silo, experiences respiratoy distress. The immediate reaction may vary from bronchitis to pulmonary edema. Therapy consists of airway maintenance, respiratory support, bronchodilators, and, in severe cases, steroids.[25] The patient may enter an asymptomatic state only to experience rapidly progressive respiratory insufficiency 10 to 30 days later. Most patients recover fully and have normal pulmonary function tests, unless they had preexisting lung disease or survived despite severe bronchiolar damage.

Environmental Exposure

In addition to the agents already mentioned, various environmental factors are involved in the health of agricultural workers.

Prolonged exposure to solar radiation is an etiologic factor in the development of solar keratosis and squamous cell carcinoma of the skin. Any patient involved in agricultural work should be closely examined for such lesions on exposed surfaces.

The farmer is often required to work under severe weather conditions. Sunstroke accounts for a significant portion of agriculture-related deaths in the southwestern United States.[26] The dangers of frostbite and exposure are well-known to the rural population of the northern states.

Chronic exposure to field dust and the vibration and noises of machinery may produce physical impairment to farm machinery operators. Lightning injuries are an infrequent but often fatal hazard to farmers.

Finally, in many areas the lack of immediate availability of skilled health care personnel may contribute to an increased incidence of death and disability.

Conclusion

The multiple disease processes that are unique to agricultural workers have been reviewed. The widespread geographic distribution and the diversity of the industry make the implementation of comprehensive preventive medicine programs difficult. Because of this, the main responsibility for preventive agricultural medicine rests upon the individual physician. He should be familiar with the various pesticides used and the diseases affecting livestock in his locality. He should be aware of the hazards inherent in prescribing medication (sedatives, anticoagulants) to this group of patients. Working together with other health and safety professions, he can maintain the health and welfare of this important segment of society.

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4-26. Will be found on page 583.

The Aging Eye

F. C. WUEST, M.D.;*† K. D. SAYTHER, M.D.;* C. A. CARLSON, M.D.;* and
P.E. WICKLUND, M.D.*‡

The problems of the aging eye include diminished vision, ocular discomfort, and cosmetic changes. Cataract, glaucoma, retinal degenerations and vascular-occlusion cause visual problems, but red eyes, epiphora or sagging lids may be just as disturbing.

THE EYE IS AS LIABLE to aging as any other organ. Most septuagenarians enjoy excellent visual function. Good vision may persist, only slightly diminished, to ages one hundred and older.

This paper describes a few problems brought on by age. They involve loss of visual function, change of cosmetic appearance, and loss of comfort. Decrease in vision is often tolerable to people beyond retirement age.

Acute vision is no longer critical as visual requirements diminish. Consider the truck driver and the accountant during their wage-earning years, and then again in retirement when driving and calculating become less frequent and less important to that person's life. Vision levels of 20/40 to 20/50 can be quite comfortable for most elderly people. A driver's license is still available to them. At vision levels of 20/70 and less, however, problems begin. Television viewing becomes difficult, acquaintances cannot be recognized until nearby, bus numerals are not easily identified, and some dependency creeps into the person's life.

At the small-print-equivalent of 20/70 (about Jaeger 7) reading becomes difficult and another of life's pleasures begins to fade. Strong reading glasses, hand magnifiers and other optical appliances offer some help; but the resilience and adaptability of youth and middle age are gone, and the difficulties in using these visual aids often outweigh their usefulness.

Physical Changes of Aging

Cornea

Arcus senilis is common in the older eye. It is an annular infiltration of lipoid material, not cholesterol, about one millimeter wide inside the limbus. It is not a degenerative phenomenon, but may be seen in certain familial lipidemias. More commonly, there is no correlation with any systemic condition.

Anterior Chamber

The anterior chamber will narrow progressively as the patient ages. This is caused by a gradual enlargement of the lens. The lens in an eighty-year-old may be three times the size of a newborn's lens. The shallowing of the anterior chamber and narrowing of the chamber angle are usually of no significance. However, in far-sighted eyes the gradual narrowing may eventuate in an acute closed-angle glaucoma. This condition is rare in myopic eyes and in patients under sixty years of age. This is of significance to the physician interested in a better view of the fundus obtained by pupillary dilation.

Lens

The most frequent cause of visual loss in the aged is the formation of a cataract. Some evidence of beginning cataract formation is almost universally present by age sixty. With age, the lens loses its clarity and assumes a yellowish-brown tinge. This is nuclear sclerosis and indicates the beginning of a senile cataract. The vision can still be 20/20 and remain so despite further progression of color change. Simultaneously a compaction of the lens occurs, causing a change in refractive power. This causes an increasing myopia or diminishing hypermetropia. As these changes progress, visual loss occurs. Other types of cataract formation are cortical spokes and posterior subcapsular opacities. Cortical cataracts radiate from the periphery toward the center of the lens and cause serious visual loss only at a relatively advanced stage. The posterior subcapsular cataract may cause diminution of reading vision without affecting distance vision in its early stages. Both the spokes and the subcapsular opacity are easily seen against the red reflex of the fundus on ophthalmoscopy.

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The only successful cataract therapy has been surgical removal of the lens, a procedure with few complications and a success ratio of well over 95%. The surgery of cataracts has changed considerably over the years. Finer suture material, more sutures, and better wound apposition result in early ambulation and fewer wound complications.

Most patients ambulate within the first postoperative day and the period of hospitalization has been remarkably shortened. Techniques of extraction have also changed. A digestive enzyme, alpha-chymotrypsin, may be used. This dissolves the zonules facilitating the removal of the lens.

Many surgeons perform cataract extractions by grasping the lens with a special forceps and tumbling it from behind the iris. Recently a cryoprobe has been used with considerable success. It forms an adherent ice ball within the lens which is then removed with less risk of capsular rupture or vitreous loss. A still newer method, applied to carefully selected types of cataract, is that of phaco-emulsification in which the lens is simultaneously emulsified and aspirated. This is done through a small opening in the peripheral cornea and allows energetic early ambulation.

Most cataract surgery is performed under local anesthesia. The post-surgical period is usually easily tolerated. A scratchy sensation is the most frequent complaint. In general, any patient who needs the surgery, and desires it, is a suitable candidate. Age alone is no contraindication. Several years ago we removed one cataract from a deeply blind woman ninety-eight years old who then lived another four years, greatly pleased with her aphakic vision.

Surgical indications vary with the patient's visual needs. At one time, surgery was delayed until a lens was "ripe" or mature. This is no longer true but the axiom still remains. Today surgery is performed when the patient is handicapped in his occupation or unhappily compromised in his ability to read, sew or perform any desired activities.

Vitreous

The vitreous is the source of very few complaints. The commonest is that of a newly observed speck or web near the visual axis. Visual acuity may vary but generally is unchanged. On ophthalmoscopy, vitreous floaters are usually seen. Occasionally this is due to the aging, liquifying vitreous separating from its fixed attachments. When the new floater is associated with flickering light streaks or flashes (photopsia) seen with movement of the head or eye and seen with the eyes open or closed, the physician must regard this complaint with a high index of suspicion of more serious disease. The most frequent cause of this symptom complex is still vitreous detachment. One must be aware that this is also commonly an early symptom of retinal detachment. Discovered, and treated while small and localized, or better yet, a retinal hole without detachment, the prognosis is excellent.

Retina

The aging retina plays host to a number of serious, potentially blinding conditions. Senile macular degeneration is the most common, affecting about 30% of people 65 years and older. Early, there is little or no visual loss. However in its severe form, it causes disabling blindness with vision of 20/200 or less. Characteristically, only the macular area is affected, resulting in a dense central scotoma. These patients have normal peripheral vision. Thus, while legally blind, these patients are not totally disabled and are able to care for themselves, take walks, and even go shopping alone. Very few use the white cane. Unfortunately, it is the sharp reading vision which is lost and the patient is sorely tried in his attempts at reading, sewing and recognizing people.

Treatment is discouraging. Vasodilators have been used but without success. Corticosteroids offer no relief. Treatment is limited to the psyche of the patient, reassuring him that he'll "never go blind." The greatest need is for reading assistance. However, to assist him with near-low vision aids meets with only limited success. None of the methods are easy to use and the older patient is easily discouraged and may even refuse to make use of the magnification.

Diseases and Other Conditions Associated with the Aging Eye

Diabetic Retinopathy has become the leading

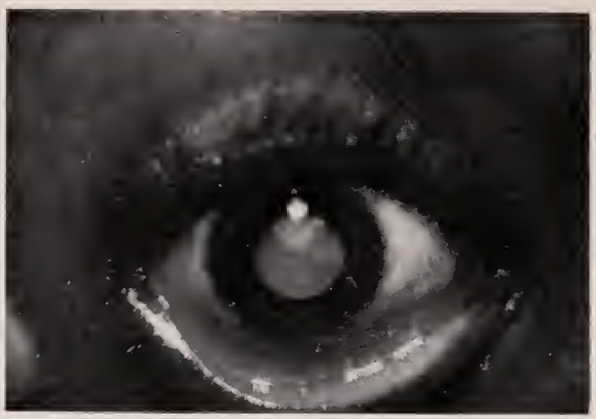

Fig. 1—Mature cataract. Note the darker gray cortical water clefts.

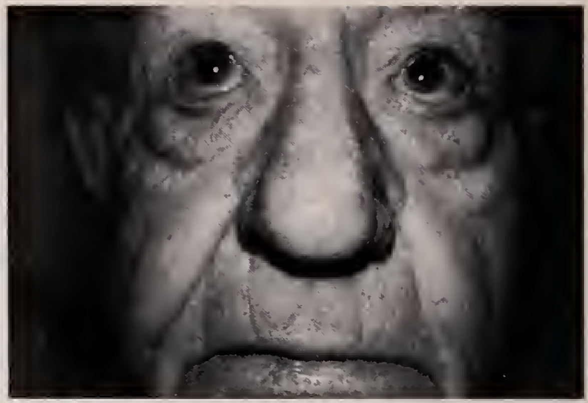

Fig. 2—Senile ectropion. Note the watery eyes, an ever present complaint. Patient has orbital fat prolapsed into lids through defects in the orbital septum.

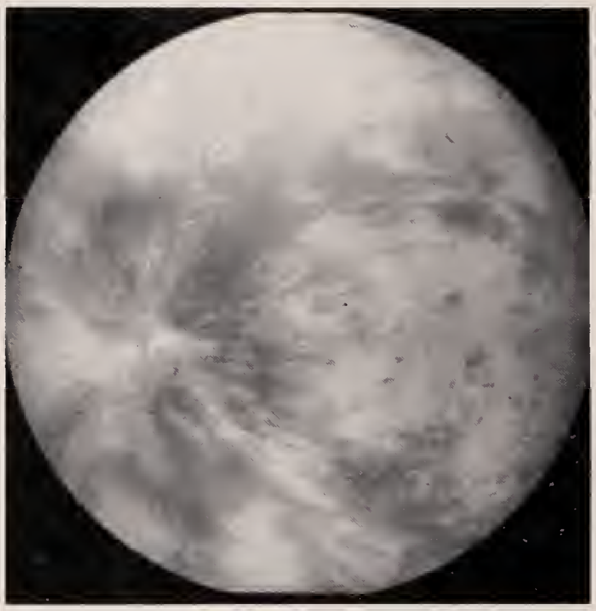

Fig. 3—Central retinal vein occlusion. Massive hemorrhages radiate out from an almost obscured optic disc. Note the greatly engorged tortuous veins.

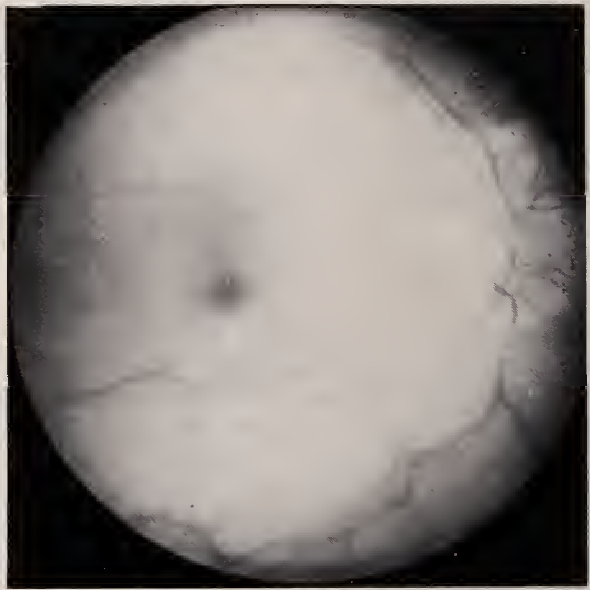

Fig. 4—Central retinal artery occlusion showing extensive retinal edema and a characteristic cherry red fovea.

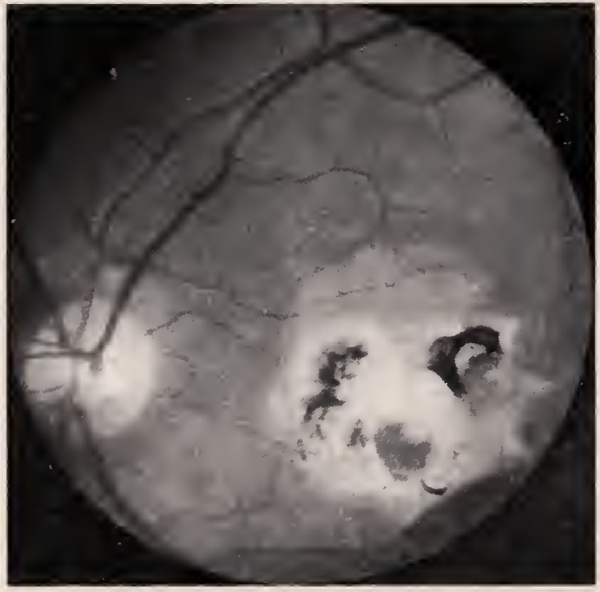

Fig. 5—Senile Macular Degeneration. The entire macula is replaced with glial tissue and pigment clumps.

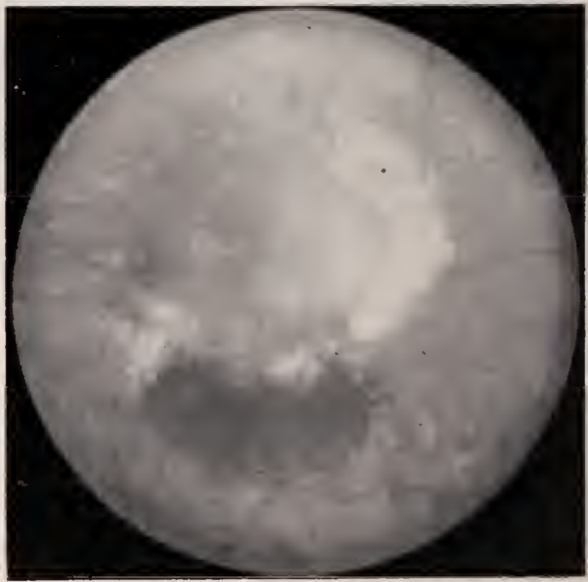

Fig. 6—Senile Macular Degeneration. Most of the macula is elevated. Note the orientation of the exudates (circinate retinopathy) and subretinal hemorrhage.

cause of blindness in the United States, overtaking glaucoma for that dubious honor. It is almost always progressive in its course. Owing to the steadily increasing longevity of diabetics, the frequency of retinopathy has increased. The condition occurs whether or not diabetic control has been good and occurs generally in two forms. In the majority of cases, termed simple diabetic retinopathy, we see microaneurysms, blot hemorrhages, and hard lipid exudates.

This form of the disease pursues a slowly progressive course often without significant visual or functional loss for decades. The second type, proliferative diabetic retinopathy, may be superimposed on the more benign type. It is characterized by neovascular proliferation in the retina and into the vitreous. Large recurrent vitreous hemorrhages, retinal cicatrization and detachment mark the last stages of this disease.

Perhaps the most promising form of ocular therapy has come with the advent of the laser. Techniques using laser and light photocoagulation are currently being evaluated regarding their long-term effectiveness in altering the course of diabetic retinopathy.

Retinal detachment is by no means limited to the aged, but its incidence increases with the years. The symptoms are typical and often alarming—beginning with flickering flashes of light in the periphery of the visual field and a sudden increase in the number of floaters. Frequently a patient will complain of a spider web or "lace doily" in the line of vision. This is followed by a descending black curtain blotting out all vision. Surprisingly, the entire sequence can occur without complaint or notice. Early diagnosis is essential to good prognosis. With early detachment, successful treatment may be accomplished by photocoagulation or external cryopexy. These procedures are rapid, safe, and can even be done as an out-patient.

Once detachment has progressed, more extensive surgical intervention becomes necessary. Great strides in surgical techniques have improved the prognosis. Basically, the retinal hole must still be sealed. An indentation in the choroid is often necessary to reappose retina to choroid and can be achieved by buckling the sciera upon itself or by using an implant on the surface of the globe. Failure may occur and multiple surgeries are sometimes necessary. A good result can be defined as a re-attached retina, not necessarily with restoration of vision. A permanently detached retina will eventually result in a phthisical, uncomfortable non-cosmetic eye often requiring enucleation.

Occlusion of the central retinal artery is dramatic and catastrophic. Visual loss is sudden and often complete. Vision will fall to bare perception of hand movements. Since it is painless, some patients may not notice its onset, while others, more perceptive, will recognize it immediately. Unfortunately, to be effective, therapy must be instituted within minutes, since retinal tissue undergoes rapid ischemic autolysis. Examination of the eye will reveal a slightly dilated pupil, reacting poorly to light. The retina will appear pale and boggy and a classical cherry-red macula will be evident. All the vessels will be attenuated, and box-carring may be evident in the arterioles. Within a few days, the vessels may resume a normal appearance but the retinal edema may remain for several weeks or months. Therapy is aimed at dilating the artery and allowing the embolus to travel further out the arteriolar tree. Immediate first-aid type treatment consists of rebreathing into a paper bag. This will increase the carbon dioxide content of the blood, producing vasodilation. In the office, a retrobulbar injection of Xylocaine without adrenalin may be given. Locally, massage of the globe or paracentesis of the anterior chamber to soften the eye is sometimes effective. Amyl Nitrate inhalation may also be used. Usually, however, the patient seeks medical aid long after any therapy can be effective and the only treatment available is consolation.

Venous occlusion presents in a similar painless fashion although the onset may be gradual as the lumen of the vein slowly closes. The occlusion is often due to external pressure on the vein such as caused by a crossing artery. Visual loss may be gradual, over a period of weeks, and if noticed by the patient, appropriate therapy may alter the course. The retinal appearance is one of countless large and small retinal hemorrhages with purplish distended veins. If vision is still better than 20/100 and only scattered hemorrhages are seen, the diagnosis of incipient vein occlusion should be entertained and therapy with anti-coagulants may be instituted.

Branch occlusions of the retinal arteries and veins also occur. They are rarely noted unless the macula is involved with concomitant loss of central vision. Usually a quadrantic sector-shaped scotoma is present which is rarely noticed by the patient and causes no handicap.

Glaucoma

While glaucoma is not restricted entirely to the aged, various surveys have indicated that between one and two-percent of the population over forty have glaucoma, and that the incidence increases with age. The frequency has been found to be as high as 13% in those over seventy-four years, an astonishing percentage which emphasizes the importance of annual checks of intraocular pressure in the elderly.

Glaucoma occurs principally in two forms. The most frequent is the chronic simple open angle glaucoma, the so-called "thief in the night" . . . which is painless and asymptomatic in its course until major damage and visual loss have already happened. It occurs as a result of thickening or sclerosis of the trabecular meshwork causing an increased resistance to the outflow of aqueous. The more dramatic, quickly painful, symptomatic type of glaucoma is the acute closed-angle glaucoma. Here the entire chamber angle is occluded by a pushed-forward iris, causing a rapid rise of intraocular pressure.

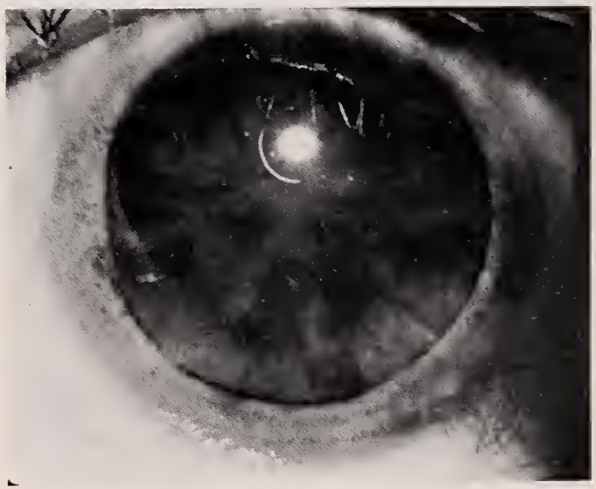

Fig. 7—Dense cataract with some brunescent nuclear sclerosis.

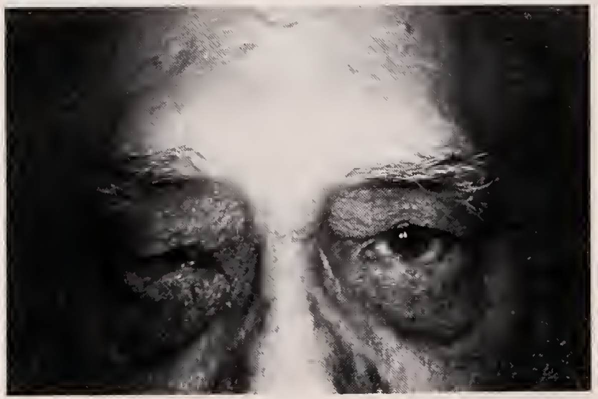

Fig. 8—Spastic entropion. Note that the lower lid margins are inverted with the lashes brushing the globe.

Most patients with chronic simple glaucoma are not disturbed by the condition as much as by the therapy. Treatment consists of topical pilocarpine or similar drugs. These cause an intense ciliary spasm and a miotic pupil. The patient may experience transient blurring of vision for up to two hours after using the drops. The miotic pupil allows less light into the eye and the patient lives in a perpetual twilight. Since the elderly may also have some lens opacities, the small pupil often accentuates the visual disability of a cataract. If epinephrine is used alone or in combination with pilocarpine, the conjunctiva blanches for several hours after application but then a strong rebound phenomenon occurs and the eyes become very red and are often a social embarrassment to the patient. Diamox and other carbonic anhydrase inhibitors are sometimes used when topical therapy alone is inadequate. Uncomfortable side effects, such as tingling hands and feet, loss of appetite with an almost perpetual metallic taste, and depression, often limits the usefulness of these drugs. Renal calculi can also occur with long term use of diamox.

The treatment of hypertension may complicate glaucoma. Sometimes an elevated systemic blood pressure may maintain a sufficient pressure gradient within a glaucomatous eye to allow adequate perfusion of critical ocular tissues. With a sudden lowering of blood pressure by medical therapy, glaucomatous damage may result. Thus, without changing intraocular pressure, lowering the systemic blood pressure may produce visual field loss and cupping of the nerve head. Physicians treating hypertension should be aware of this danger. The Ophthalmologist should be notified of the therapy so that closer observation of the intraocular tension and visual fields may be instituted.

Early diagnosis of glaucoma is essential to successful management. The earlier in the course of glaucoma that the diagnosis is made, the easier the treatment and subsequent control. Good control demands constant observation and vigilance which older patients can find difficult. In general, with adequate treatment, about 70% of cases become stabilized, 20% deteriorate slowly but maintain some useful vision, while 10% ultimately are visually incapacitated.

Closed angle glaucoma develops in a variety of ways. The episode can occur suddenly without warning in an apparently healthy eye, but more often it is preceded by mild prodromal attacks which can occur intermittantly for months or years. These subacute episodes are often precipitated by dilation of the pupil and therefore usually occur in the evening. They are later relieved by miosis during sleep. Emotional disturbance, with its increased sympathetic tonus and reflex pupillary dilation, may also trigger an attack. The vision becomes hazy, halos appear around lights, and there may be a mild localized headache. Each attack is the result of functional closure of the anterior chamber angle. With repeated attacks, peripheral anterior synechiae develop and the recurring episodes become more frequent and last longer. Eventually, a permanent chronic closed angle glaucoma results, or an acute crisis may develop.

An acute attack of closed angle glaucoma invariably begins suddenly, usually in one eye, with intense pain in the eye and trigeminal area, frequently associated with nausea and vomiting, accompanied by a rapid loss of vision. This can result in permanent loss of light perception within hours. Treatment must be immediate and consists of miotic drops and hyperosmotic agents such as glycerin orally, if tolerated, or mannitol intravenously. Finally surgery, a peripheral iridectomy, may be necessary to relieve the obstructed angle. Surgery on the second eye is recommended by some since the condition is usually bilateral. If left untreated, an acute attack will probably occur in the second eye.

Cosmetic Aspects of the Aging Eye

Some of the most obvious aspects of aging around the eye are those related to the lids. With increasing age, degenerative changes and loss of elasticity occur in these tissues. Initially there is a loss of tension evidenced by baggy lids in the morning. With time, more elastic fibers are lost leaving a baggy lid and the wrinkled appearance of age. The skin and subcutaneous tissue may be so atrophic and lax that it hangs down as a fold past the lid margin. This is seldom more than a cosmetic problem. This dermachalasis can be corrected by excising the excess skin. Loss of elastic tissue can also lead to relaxation of the tarsal ligaments. The lid margin may become inverted by the unopposed action of the orbicularis muscle, resulting in an entropion. The eye lashes rubbing against the conjunctiva and cornea may cause a chronically irritated eye.

Subconjunctival hemorrhages are common in the elderly. They are characterized by the acute, painless onset of bright red blood, noticed against the white scleral background. This is only a minute amount of blood that is spread against the white sclera but its appearance is very frightening to the patient. Most commonly there is no apparent cause, although the patient may give a history of coughing, sneezing or rubbing their eyes.

Pingueculae occur in middle age as well as in the elderly. These are small, yellowish, slightly elevated areas on the conjunctiva, located close to the limbus in the interpalpebral fissure. The patient may be disturbed by the presence of the mass or may have vague sensations of irritation. A pinguecula is composed of hypertrophic and degenerated connective tissue fibers and frequently will have an increased vascular supply. When the eye is irritated or red for any other reason, this area will become more congested. The cause of these lesions is not clear but does seem to be connected with chronic irritation. There is usually no treatment necessary other than reassurance of its benign nature. Occasionally the patient is more comfortable using vaso-constricting eye drops. A similar lesion invading the cornea is called a pterygium. This usually does not require treatment but it may continue to encroach sufficiently on the cornea to require excision.

Xanthelasma are yellowish plaques located within the skin of the lids. They are flat and irregular and tend to follow skin folds. The lesions are benign lipid and histiocyte infiltrates in the dermis which may occur in patients with hypercholesteremia but are more often seen with normal serum cholesterol. They may become unsightly and require excision.

Veruccae are fleshy, multilobulated lesions with flat or pedunculated bases, frequently located at the lid margins. These are caused by a virus and are readily treated by excision of the mass and cauterization of the base. However, caution is advised if these are near the gray line of the lid margin, because too vigorous treatment may result in notching of the margin.

Milia, which are merely tiny sebaceous cysts containing keratin, are also frequently seen in the aging lid. These are easily treated by incising the overlying skin and expressing the offending material. On the conjunctival side of the lid, patients will often have numerous small white concretions. This usually is asymptomatic although occasionally these collections, which are an accumulation of inspissated mucous and epithelial cells in Henle's glands, may actually rub against the globe. With adequate magnification, these can be removed with the aid of a sharp needle. The vast majority however, are below the conjunctival surface and cause no symptoms.

Basal cell carcinoma, the most common lid neoplasm, increases in frequency with age. It occurs most commonly in the lower lid, and frequently presents as a "rodent" ulcer with a raised nodular border and indurated base. When treated early, total surgical excision gives the most satisfactory therapeutic and cosmetic result.

Loss of Comfort in the Aging Eye

The principal complaints of discomfort in the aged are usually related to dry eyes, excessive tearing or chronically injected eyes. Decreased tear formation arises either because of atrophy of the tear-producing glandular tissue or cicatricial occlusion of the orifices of tear glands. Accessory lacrimal glands and conjunctival goblet cells are primarily responsible for maintaining basal tear secretion sufficient for normal moistening of the eye. Normal senile atrophy of the conjunctiva brings about reduced tear production. Typical symptoms are burning and dryness. The condition is aggravated by warmth and dry ambient conditions which cause rapid evaporation of tears. There may be punctate epithelial erosions of the cornea and conjunctiva. Newer, mucin-like preparations offer longer-lasting symptomatic relief. Excessive tear formation is usually secondary to reflex stimulation of the lacrimal gland. Inadequate basal tear secretion results in dry eyes which then stimulate reflex tearing by the main lacrimal gland, a seemingly paradoxical situation. Excessive tearing is a nuisance since the vision is blurred and the continual overflow of tears onto the face is annoying. Irritation and infection of the cornea or conjunctiva may also cause reflex stimulation of the lacrimal gland, with an overproduction of tears. Abnormal regeneration of the seventh cranial nerve following facial nerve palsy may lead to tearing associated with salivation (crocodile tears) because of diversion of fibers from the salivary to the lacrimal gland. Producing the same symptoms as excessive tear formation is faulty drainage of tears. Multiple causes of this exist, including poor apposition of the lacrimal punctum to the lacrimal lake, scarring of the lacrimal puncta, paresis of the orbicularis oculi muscle eliminating the suction of the canaliculi, foreign body in the canaliculi, and obstruction in the nasolacrimal sac and duct.

With generalized atrophy of elastic and fibrous tissues occurring in elderly people, one often sees baggy, relaxed eyelids of such degree that ectropion of the lid results. As the lid falls away from the globe, the inferior punctum no longer remains in contact with the lacrimal lake, resulting in epiphora. Eventually senile ectropion may be accompanied by exposure and xerosis of the palpebral and bulbar conjunctiva with symptoms of pain and irritation as well as epiphora.

Occasionally, because of the relaxed condition of the lower eyelid, the lashes may become inverted by the unopposed action of the orbicularis muscle at the lid margin. This is referred to as senile entropion, and results in chronic irritation of the conjunctiva and inferior cornea.

Herpes Zoster virus occasionally affects branches of the fifth cranial nerve, especially the ophthalmic division. These patients experience variable, but usually severe degrees of pain associated with vesicles of the brow, eyelids, and scalp. There may be involvement of the cornea, uveal tract, or even the optic nerve. These latter findings are usually present when vesicles occur near the tip of the nose, thereby indicating involvement of the nasociliary branch of the fifth cranial nerve. It is not uncommon for people to continue to experience recurring pain in and about the eyes for months or years after the acute phase of the infection.

Even though visual function may remain at a satisfactory level, symptoms of ocular discomfort, can be as distressing as poor vision. Treatment, while not always successful, should be prompt and vigorous.

References on page 583.

Famous Fighters

JOHN L. SULLIVAN
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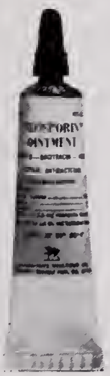
NEOSPORIN® Ointment
(polymyxin B-bacitracin-neomycin)
is a famous fighter, too.

Provides overlapping, broad-spectrum antibacterial action to help combat infection caused by common susceptible pathogens (including staph and strep).



ach gram contains: Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc acitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); pecial white petrolatum qs in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) il packets.

DICATIONS: Therapeutically (as an adjunct to systemic therapy when indicated) r topical infections, primary or secondary, due to susceptible organisms, as in: infected burns, skin grafts, surgical incisions, otitis externa • primary odermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily fected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic sions, inflamed or suppurating as a result of bacterial infection.

rophylactically, the ointment may be used to prevent bacterial contamination in urns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts d wounds accidentally incurred, its use may prevent the development of infection and permit wound healing. **CONTRAINDICATIONS:** Not for use in the eyes or ternal ear canal if the eardrum is perforated. This product is contraindicated in ose individuals who have shown hypersensitivity to any of the components. **ARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended. **PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. **ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.

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Proven Cholesterol-Lowering Adjunct to Diet.

n effective agent for low density lipoproteins in uthyroid, Non-Cardiac Patients.

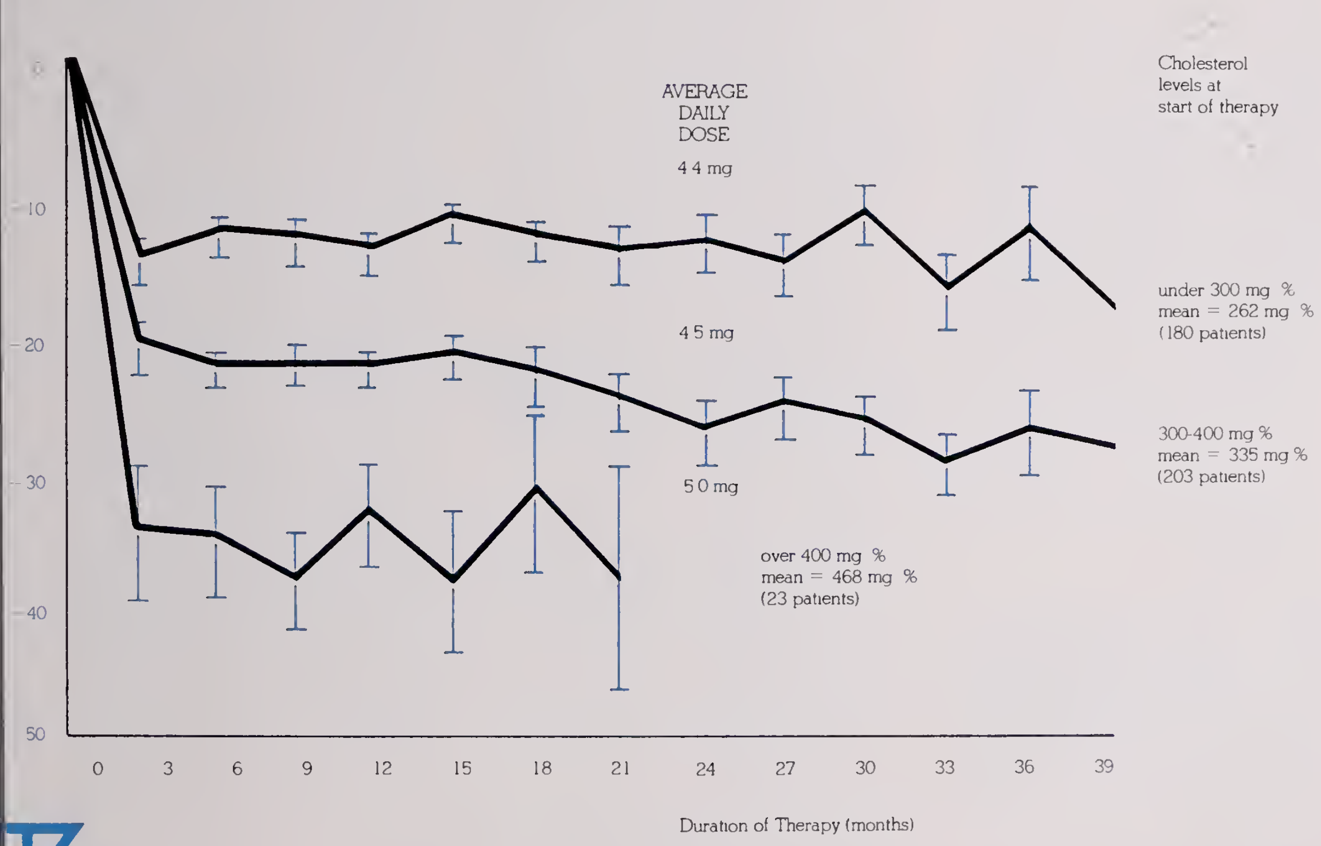
HOLOXIN® (Sodium Dextrothyroxine) is the con-nient and practical way to manage the hard-to-nage patient who doesn't always follow the diet gimen that you've outlined.

onvenient once-a-day dosage encourages patient operation, and it's economical for long-term erapy.

AN IMPORTANT NOTE:
It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question.

CHOLOXIN (Sodium Dextrothyroxine) is a thyroid analogue which effectively lowers elevated serum cholesterol 15 to 35% (see chart below) in low density lipoproteins.

CHOLOXIN (Sodium Dextrothyroxine) has undergone ten years of clinical trials and seven years of practice. The clinical trials consisted of 337 clinical studies involving over 3,000 hypercholesterolemic non-cardiac patients. It is among the most thoroughly evaluated drugs ever presented to physicians.



NOT ALL PATIENTS ARE REPRESENTED AT EACH TIME INTERVAL

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NOTE:
See following page for full prescribing information.

Choloxin

(Sodium Dextrothyroxine)

Effectively Lowers Elevated Cholesterol With Convenient Once-A-Day Dosage

Four strengths... 1, 2, 4, and 6 mg.... are available making the scored tablet regimen a flexible dosage system. And, for most patients, CHOLOXIN tablets offer once-a-day dosage.

CHOLOXIN* (sodium dextrothyroxine) Single-Tablet-A-Day Dosage Schedules

See prescribing information in package insert reproduced below

	Starting Dosage	**Increased Monthly by**	**Usual Maintenance**	**Maximal Recommended**
Adult Hypercholesterolemic	1 0-2.0 mg	1 0-2 0 mg	4 0-8 0 mg	4 0-8 0 mg
Pediatric Hypercholesterolemic	0 05 mg /kg body weight	0 05 mg /kg	0 1 mg /kg body weight	4 0 mg
Hypothyroid Cardiac	0 5-1 0 mg	1 0 mg	4 0 mg	4 0 mg

Description

CHOLOXIN (sodium dextrothyroxine) is the sodium salt of the dextrorotatory isomer of thyroxine It is chemically described as D-3,5,3' 5'-tetraiodothyronine sodium salt

Actions

The predominant effect of CHOLOXIN (sodium dextrothyroxine) is the reduction of serum cholesterol levels in hyperlipidemic patients Beta lipoprotein and triglyceride fractions may also be reduced from previously elevated levels

Most of the available evidence indicates that CHOLOXIN stimulates the liver to increase catabolism and excretion of cholesterol and its degradation products via the biliary route into the feces Cholesterol synthesis is not inhibited and abnormal metabolic end-products do not accumulate in the blood

Indications

This is not an innocuous drug Strict attention should be paid to the indications and contraindications.

CHOLOXIN (sodium dextrothyroxine) is an antilipidemic agent used as an adjunct to diet and other measures for the reduction of elevated serum cholesterol (low density lipoproteins) in euthyroid patients with no known evidence of organic heart disease

The drug is also indicated in the treatment of hypothyroidism in patients with cardiac disease who cannot tolerate other types of thyroid medication **Before prescribing, note the following: Results from a randomized clinical study have indicated a possible adverse effect when CHOLOXIN (sodium dextrothyroxine) is administered to a patient receiving a digitalis preparation. There may be an additive effect. This additive effect may possibly stimulate the myocardium excessively in patients with significant myocardial impairment CHOLOXIN (sodium dextrothyroxine) dosage should not exceed 4 mg per day when the patient is receiving a digitalis preparation concomitantly. Careful monitoring of the total effect of both drugs is important.**

It has not been established whether the drug-induced lowering of serum cholesterol or lipid levels has a detrimental, beneficial, or no effect on the morbidity or mortality due to atherosclerosis or coronary heart disease. Several years will be required before current investigations will yield an answer to this question.

Contraindications

The administration of CHOLOXIN (sodium dextrothyroxine) to euthyroid patients with one or more of the following conditions is contraindicated

1 Known organic heart disease including angina pectoris, history of myocardial infarction, cardiac arrhythmia or tachycardia either active or in patients with demonstrated propensity for arrhythmias rheumatic heart disease history of congestive heart failure and decompensated or borderline compensated cardiac status
2 Hypertensive states (other than mild labile systolic hypertension)
3 Advanced liver or kidney disease
4 Pregnancy
5 Nursing mothers
6 History of iodism

Warnings

CHOLOXIN (sodium dextrothyroxine) may potentiate the effects of anticoagulants on prothrombin time. Reductions of anticoagulant dosage by as much as 30% have been required in some patients. Consequently, the dosage of anticoagulants should be reduced by one-third upon initiation of CHOLOXIN (sodium dextrothyroxine) therapy and the dosage subsequently readjusted on the basis of prothrombin time. The prothrombin time of patients receiving anticoagulant therapy concomitantly with CHOLOXIN (sodium dextrothyroxine) therapy should be observed as frequently as necessary, but at least weekly, during the first few weeks of treatment

In the surgical patient it is wise to consider withdrawal of the drug two weeks prior to surgery if the use of anticoagulants during surgery is contemplated

When CHOLOXIN (sodium dextrothyroxine) is used as thyroid replacement therapy in hypothyroid patients with concomitant coronary artery disease (especially those with a history of angina pectoris or myocardial infarction) or other cardiac disease treatment should be initiated with care Special consideration of the dosage schedule of CHOLOXIN (sodium dextrothyroxine) is required This drug may increase the oxygen requirements of the myocardium especially at high dosage levels Treated subjects with coronary artery disease must be seen at frequent intervals If aggravation of angina or increased myocardial ischemia cardiac failure or clinically significant arrhythmia develops during the treatment of hypothyroid patients the dosage should be reduced or the drug discontinued

Special consideration must be given to the dosage of other thyroid medications used concomitantly with CHOLOXIN (sodium dextrothyroxine) As with all thyroactive drugs, hypothyroid patients are more sensitive to a given dose of CHOLOXIN (sodium dextrothyroxine) than euthyroid patients

Epinephrine injection in patients with coronary artery disease may precipitate an episode of coronary insufficiency This condition may be enhanced in patients receiving thyroid analogues These phenomena should be kept in mind when catecholamine injections are required in sodium dextrothyroxine-treated patients with coronary artery disease

Since the possibility of precipitating cardiac arrhythmias during surgery may be greater in patients treated with thyroid hormones it may be wise to discontinue CHOLOXIN (sodium dextrothyroxine) in euthyroid patients at least two weeks prior to an elective operation During emergency surgery in euthyroid patients and in surgery in hypothyroid patients in whom it may not be advisable or possible to withdraw therapy the patients should be carefully observed

There are reports that sodium dextrothyroxine in diabetic patients is capable of increasing blood sugar levels with a resultant increase in requirements of insulin or oral hypoglycemic agents Special attention should be paid to parameters necessary for good control of the diabetic state in dextrothyroxine-treated subjects and to dosage requirements of insulin or other antidiabetic drugs If sodium dextrothyroxine is later withdrawn from patients who required an increase of insulin (or oral hypoglycemic agents) dosage during its administration the dosage of antidiabetic drugs should be reduced and adjusted to maintain good control of the diabetic state

When either or both impaired liver or kidney function are present the advantages of CHOLOXIN (sodium dextrothyroxine) therapy must be weighed against the possibility of deleterious results

Usage in Women of Childbearing Age

Women of childbearing age with familial hypercholesterolemia or hyperlipemia should not be deprived of the use of this drug it can be given to those patients exercising strict birth control procedures Since pregnancy may occur despite the use of birth control procedures administration of CHOLOXIN (sodium dextrothyroxine) to women of this age group should be undertaken only after weighing the possible risk to the fetus against the possible benefits to the mother Teratogenic studies in two animal species have resulted in no abnormalities in the offspring

Precautions

It is expected that patients on dextrothyroxine therapy will show greatly increased serum protein bound-iodine levels These increased serum PBI values are evidence of absorption and transport of the drug and should NOT be interpreted as evidence of hypermetabolism similarly they may not be used for titrating the effective dose of CHOLOXIN (sodium dextrothyroxine) PBI values in the range of 10 to 25 mcg% in treated patients are common

If signs or symptoms of iodism develop during CHOLOXIN (sodium dextrothyroxine) therapy the drug should be discontinued

A few children with familial hypercholesterolemia have been treated with CHOLOXIN (sodium dextrothyroxine) for periods of one year or longer with no adverse effects on growth However it is recommended that the drug be continued in patients in this age group only if a significant serum cholesterol-lowering effect is observed

Adverse Reactions

The side effects attributed to dextrothyroxine therapy are for the most part due to increased metabolism and may be minimized by following the recommended dosage schedule Adverse effects are least commonly seen in euthyroid patients with no signs or symptoms of organic heart disease The incidence of adverse effects is increased in hypothyroid patients and is highest in those patients with organic heart disease superimposed on the hypothyroid state

In the absence of known organic heart disease some cardiac changes may be precipitated during sodium dextrothyroxine therapy In addition to angina pectoris arrhythmia consisting of extrasystoles ectopic beats or supraventricular tachycardia ECG evidence of ischemic myocardial changes and increase in heart size have been observed Myocardial infarctions both fatal and non-fatal have occurred but these are not unexpected in untreated patients in the age groups studied It is not known whether any of these infarcts were drug related

Changes in clinical status that may be related to the metabolic action of the drug include the development of insomnia nervousness palpitations tremors loss of weight lid lag sweating flushing hyperthermia hair loss diuresis and menstrual irregularities Gastrointestinal complaints during therapy have included dyspepsia nausea and vomiting constipation diarrhea and decrease in appetite

Other side effects reported to be associated with CHOLOXIN (sodium dextrothyroxine) therapy include the development of headache, changes in libido (increase or decrease), hoarseness, tinnitus dizziness, peripheral edema malaise tiredness visual disturbances psychic changes paresthesia muscle pain and various bizarre subjective complaints Skin rashes including a few which appeared to be due to iodism, and itching have been attributed to dextrothyroxine by some investigators Gallstones have been discovered in occasional dextrothyroxine-treated patients and cholestatic jaundice has occurred in one patient although its relationship to CHOLOXIN (sodium dextrothyroxine) therapy was not established

In several instances the previously existing conditions of the patient appeared to continue or progress during the administration of CHOLOXIN (sodium dextrothyroxine), a worsening of peripheral vascular disease sensorium exophthalmos and retinopathy have been reported

CHOLOXIN (sodium dextrothyroxine) potentiates the effects of anticoagulants such as warfarin or Dicumarol, on prothrombin time thus indicating a decrease in the dosage requirements of the anticoagulants On the other hand dosage requirements of antidiabetic drugs have been reported to be increased during dextrothyroxine therapy (see WARNINGS section)

Dosage and Administration

For **adult** euthyroid hypercholesterolemic patients the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is 4 to 8 mg per day The initial daily dose should be 1 to 2 mg to be increased in 1 to 2 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily if that dosage level is indicated to effect the desired lowering of serum cholesterol

When used as partial or complete substitution therapy for levothyroxine in hypothyroid patients with cardiac disease who cannot tolerate other types of thyroid medication, the initial daily dose should be 1 mg to be increased in 1 mg increments at intervals of not less than one month to a maximum level of 4 to 8 mg daily preferably the lower dosage The maximum in patients receiving digitalis therapy is 4 mg

For **pediatric** hypercholesterolemic patients the recommended maintenance dose of CHOLOXIN (sodium dextrothyroxine) is approximately 0 1 mg (100 mcg) per kilogram The initial daily dosage should be approximately 0 05 mg (50 mcg) per kilogram to be increased in up to 0 05 mg (50 mcg) per kilogram increments at monthly intervals The recommended maximal dose is 4 mg daily if that dosage is indicated to effect the desired lowering of serum cholesterol

If new signs or symptoms of cardiac disease develop during the treatment period the drug should be withdrawn

How Supplied

CHOLOXIN (sodium dextrothyroxine) is supplied in prescription packages of scored 1 2 4 and 6 mg tablets

March 1975

FLINT LABORATORIES
DIVISION OF TRAVENOL LABORATORIES, INC.
Deerfield, Illinois 60015

Editorials

Omphaloskepsis and Other Umbilical Phenomena

When someone looks at anything, it's nothing or a many-thing
The eyes of the beholder make it trivial or great
Soloman without a flicker called it "globlet full of liquor"
And for the umbilicus this is very high estate.
William B. Bean, M.D.,
"Omphaloscopy and Worse Verse,"
Read before the American Clinical
and Climatological Association,
Hot Springs, Virginia, 1953

OMPHALOSKEPSIS, FOR those of you not in the know, is an important phenomena. So important that only a small cult in India practices it. Omphaloskepsis is, of course, meditating while gazing at one's navel.

In any event, the excellent article of Key*, Shephard, and Walters in this issue brings omphaloskepsis to mind. The authors tell the story of Sister Mary Joseph of the Mayo Clinic and of her observation that umbilical nodules may signal the presence of abdominal carcinoma. I advise you to read the article for its historical value and for its clear description of a remarkable woman.

I also bring omphaloskepsis to your attention because I'm one of those dwindling few who believe the umbilicus occupies a central place in human events. Consider the exotic dancer. If you should happen to be watching her perform, her more mobile parts will distract you, and you will not appreciate her art. For absolute concentration (and meditation), keep your eye on the umbilicus.

As a former basketball player, I can also inform you one of the cardinal defensive rules of that game is to fix your gaze on the offensive man's umbilicus. Where it goes, he goes. I'm sure the same rule applies to girls' basketball too.

The important thing here is not that Key et al.'s fine article, omphaloskepsis, exotic dancing, basketball and the umbilicus are associated. The important thing is this: *Concentrate on the umbilicus, and nothing will distract you.*

Richard L. Reece, M.D.
Editor-in-Chief

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*See page 561.

Spectrum of Agricultural Medicine

A VERY TIMELY PUBLICATION "The Spectrum of Agricultural Medicine," appears in this issue.* It is especially appropriate for this time of the year because the workers in agriculture are most active now. The article succinctly describes, "five major kinds of problems in Agricultural Medicine": (1) Farm Accidents, (2) Infectious Diseases, (3) Chemical Toxicity, (4) Respiratory Conditions, and (5) Environmental Exposure.

The rural practitioner of medicine may encounter a greater variety of medical problems than his urban colleague. His knowledge must be broad to encompass the five problem areas, especially in chemical toxicity which is an ever increasing health hazard among agricultural workers, generally not trained to handle these chemicals. His skill coordinated, when indicated, with those of his colleagues and working with them and other health and safety professionals will do much to "maintain the health and welfare of this important segment of society."

The problems of Agricultural Medicine are not limited to the rural population, indeed, they are public health problems affecting our entire society. For example, the zoonoses infecting the agricultural worker can also infect the general population. The development of programs for the prevention and control of the zoonoses begins with the practicing physician, he is on the front line of battle for better public health, he is first to see the infected person. It is through his reports that we get information of public health problems, the need to develop programs to combat the problems, and the success or failure of such programs.

The first Institute of Agricultural Medicine, within the framework of a Medical School, was established in 1952 at the University of Iowa in Iowa City by Franklin H. Top, Sr., M.D., M.P.H. Some may remember Dr. Top who prior to establishing the Institute, was a professor of epidemiology, School of Public Health, University of Minnesota in Minneapolis.

It is an enigma that more physicians do not seek the challenges of a rural practice and that Agricultural Medicine is not given greater emphasis in the medical schools of the agricultural midwest.

Henry Bauer, Ph.D.†
Minneapolis, Minnesota

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*See page 536.

†Director, Division of Medical Laboratories, Minnesota Department of Health, Minneapolis, Minnesota.

"Silent Thyroiditis" Versus Thyrotoxicosis Factitia

IN PATIENTS WHO present with hyperthyroxinemia, hypermetabolism, and a blocked ^{131}I uptake, the differential diagnosis includes subacute thyroiditis in its overt or "silent" variants, iodide-induced thyrotoxicosis, Graves' disease with severe iodine overload, thyrotoxicosis factitia, and lymphocytic thyroiditis accompanied by extensive follicular disruption and inappropriate release of thyroid hormone into the bloodstream. In the last named condition, hyperthyroidism should terminate when the hormone stores are exhausted, and transient hypothyroidism may follow until the follicular epithelium has healed and hormone synthesis has been restored. Such a course has been observed in the patients with this syndrome already reported.[1,2] Typically, subacute thyroiditis is a painful disease.

The diagnosis of the other conditions described above and of silent subacute thyroiditis rests on meticulous thyroid function testing and thyroid biopsy. In defining a new syndrome, rigorous proof must be presented that other known similar diseases have been excluded. The presence of a goiter does not by itself exclude malingering. Urinary iodide measurements are needed to exclude iodide overload. If needle biopsy is performed, the timing must be such that granulomatous thyroiditis will be clearly excluded. The core of tissue on needle biopsy should be representative of the gland as a whole.

In the June issue, Hofeldt et al.,* describe a patient who may have the goitrous transient hyperthyroidism of lymphocytic thyroiditis. Their patient conforms to those already described in having minimal or no elevation of the erythrocyte sedimentation rate or thyroglobulin antibody titer. The authors do not specify the duration of the hyperthyroid phase of the patient's illness. Biopsy from both thyroid lobes established the presence of a destructive lymphocytic thyroiditis.

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*See page 380.

The radioiodine uptake test plays a critical role in the diagnosis of this condition. Fortunately for practicing physicians, an extensive evaluation may not be necessary. Patients with painless thyroid enlargement, hyperthyroxinemia, and a blocked ^{131}I uptake should be checked for iodide overload by urine ^{127}I measurement and taking an appropriate history. If none is found, the patient's symptoms may reasonably be controlled with propranolol and spontaneous recovery may be expected in a matter of weeks. If recovery does not occur within the space of four to six weeks, further testing may be done for iodine-loaded Graves' disease, struma ovarii, or thyroid malingering.

Colum A. Gorman, M.B., B.Ch.
Rochester, Minnesota

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Caloric Intake of Patients with Advanced Cancer

MAINTAINING ADEQUATE nutritional intake in patients with chronic diseases are, at times, difficult problems. Illness, if sustained, seems to decrease the desire for food. Inactivity, as well as various treatment modalities (surgery, radiation therapy and chemotherapy) are contributing factors for the decreased caloric intake of chronically ill patients. Altered and diminished taste sensitivity seems to cause additive problems.

The physician, in attempting to maintain adequate nutrition, may employ intravenous supplementation, or hyperalimentation in an attempt to correct nutritional defects. Nursing and dietary help to prepare and administer adequate foods that are appealing to the patients are generally employed. Very little is known as to why patients with lingering diseases decrease their caloric intake. Depression, inactivity, as well as a direct metabolic effect by the tumor have been implicated as etiologic factors.

In patients with cancer, cachexia[2] seems to decrease the safety margin of most chemical agents employed in therapy.[1] As the tumor grows, it seems to consume increasing amounts of glucose at the metabolic expense of the host. As a result, hypoalbuminemia and a negative nitrogen balance is frequently seen.[2] It has been postulated that if debilitated patients with cancer can be repleted nutritionally, they may be better able to tolerate therapy.

In this issue, Theologides et al.* explore the nutritional habits of patients with cancer. They have documented both anorexia and oligophagia in cancer patients but feel both food preferences and meal patterns are retained.

It would be valuable to know more about why these patients become anorexic, and of greater value in knowing how to correct this. Also, we need to know whether correcting the nutritional abnormalities will favor the overall prognosis. Much needs to be learned about tumor metabolism as it affects host resistance and how this blends into the total therapy in patients with cancer.

Neil Hoffman, M.D.
Minneapolis, Minnesota

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*See page 526.

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2. Gold J: Proposed treatment of cancer by inhibition of gluconeogenesis. Oncology 22:185, 1968.

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Laboratory Tests in Coagulation Screening

PRESURGICAL SCREENING for a potential bleeding problem has always been a favorite topic between surgeons and laboratory workers. In this issue of MINNESOTA MEDICINE, there is an excellent review article by John O. Swanson,* from Metropolitan Medical Center, Clinical Laboratory. It deals with the common "Routine" laboratory tests recommended to be used to identify the cause of bleeding problems when they appear, as well as a discussion of which tests are best to perform prior to surgery in order to avoid catastrophic bleeding during and after surgery. Our surgical colleagues and students of coagulation problems will most likely welcome the concise presentation.

It is apparent that the medical history remains the most important part of the presurgical work-up. Without proper communication between the attending physician and laboratory personnel, coagulation screening and effective resolution of a bleeding problem is very difficult if not impossible. The laboratory worker must know something about the patient being evaluated. For those who are confronted daily with bleeding problems, as is the case with the leading reference laboratories, it is much easier to follow certain established ways to establish the proper diagnosis. For those of us who are faced only occasionally with the bleeding patient, and for those who want to know which tests are best to order for "Routine Screening" it will be helpful to have this article at hand.

N. D. Kostich, M.D.
Minneapolis, Minnesota

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*See page 517.

Uterine Prolapse and Upper Urinary Tract Obstruction

DR. T. A. HILDRETH, et al., in the July issue* call our attention to a serious, yet not so uncommon disease which should be preventable. Unfortunately, there is often a delay in the recognition and treatment of upper urinary tract obstruction associated with a severely relaxed female pelvic floor.

The authors' cases illustrate two methods of management. Good results were attained by both the conservative and surgical approach. In case number two, the pessary failed, which has been my experience. Progressive deterioration of renal function and advancing age may preclude surgical correction, if the diagnosis and treatment are delayed. Early detection of hydronephrosis by IVP with upright films in the female with uterine prolapse will be rewarding.

Bruce E. Linderholm, M.D.
Minneapolis, Minnesota

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*See page 450.

Farmfest—Lake Crystal, Minnesota

Farmfest '76 has designated September 18 as Rural Health Day at Farmfest. A special medical forum will feature Dr. David Boyd, Emergency Medical Service Director of HEW. Other speakers will be announced.

Letter to the Editor

Dear Editors:

Twenty-Five Years Association of a Psychiatrist

Dr. John A. Haugen's editorial in the June 1976[*] MINNESOTA MEDICINE relative to my May 1976[†] article in MINNESOTA MEDICINE is truly appreciated.

Further research corroborated the correctness of his comments. The facts pointed out by Dr. Haugen not only emphasizes the astuteness and foresight of Dr. McKelvey, but demonstrates the value of recording in black and white one's observations as he sees them for others to confirm, correct, or deny.

Irving C. Bernstein, M.D.
Minneapolis, Minnesota

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[*] Minnesota Med 59:397, 1976.
[†] Minnesota Med 59:341, 1976.

Cover Painting
William H. Mayo, M.D., Surgeon

Dr. William H. Mayo operating in Room No. 1, St. Mary's Hospital, Rochester, Minnesota. Instrument Nurse Sister Sylvester and Anesthetist Miss Serena Huntimer.

Painted by Dr. Louis A. Buie, Sr. from a snapshot made in 1933. Dr. Buie, who died last year, founded the Department of Colon and Rectal Surgery at the Mayo Clinic, and was its Head until his retirement in 1955.

Dr. Buie's painting "South Carolina, Remembered" featured on the April, 1971, cover of MINNESOTA MEDICINE won an award as the outstanding cover for that year.

Pediatric Conferences at Children's Hospital
St. Paul, Minnesota

These conferences have been approved by the American Academy of Family Practice for Continuing Education and are held the second and fourth Thursdays from 8:30 to 9:30 a.m. in our Auditorium.

Aug. 12, 1976	"Pancreatitis"	William Brennom, M.D.
Aug. 26, 1976	"Malignant Hypertension"	Richard Gehrz, M.D. Charles Jarvis, M.D. Hugh Williams, M.D.

Health Policy

A Challenge—Health Care Cost Containment*

G. ROY DIESSNER, M.D.
Past President
Minnesota State Medical Association

Mr. Speaker, Delegates and Guests:

During the past six years, it has been customary for your President to address the House of Delegates on a subject of his choice in addition to the Report that has been referred to a Reference Committee. I welcome this opportunity and, as many of you might guess, I'd like to talk about money and costs—the costs of health care. In doing so I'd like to offer a challenge to medicine to assume *the* leadership role in the struggle to contain and limit the escalation of health care costs. If we fail to meet this challenge in a very short time, I believe legislation for the *strict* regulation of medical care costs and the practice of medicine is imminent. Whether we accept it or not, the politicians and the congress place the blame for the escalation of health care costs on the medical profession—not on the poorly conceived inflationary programs congress has legislated.

National Conference on Health Policy

Three weeks ago, I attended The National Leadership Conference on America's Health Policy sponsored in part by Congressmen Paul Rogers and Dan Rostenkowski. In recent months, these two powerful and knowledgeable chairmen of two House health subcommittees have been involved in a jurisdictional dispute regarding health legislation which has delayed attention to these pressing problems. This Conference turned out to be an attack primarily on the medical care system and was directed almost entirely at the escalation of health care costs.

A broad range of topics and speakers were heard during the two conference days—the voice of organized medicine was insignificant—the voice of the consumer (amazingly in this era of consumerism) was not heard—but the voice of bureaucracy and government at all levels (county, state, and federal) was the loudest and most clear. The themes repeatedly stressed were: (1) health care costs and medical care costs are not to be separated in considering solutions—in fact, few of the speakers seemed aware of the significant differences; (2) although all agreed that health care cost escalations began with the passage of Medicare and Medicaid ten years ago and have been further aggravated by almost every federal health program passed by Congress since, these programs are here to stay and none will be drastically curtailed or altered; (3) politicians consider themselves *blameless* for legislating programs of overpromise without understanding or heeding the inflationary pressures predicted by organized medicine—because they "were responding to the demands of their constituents"; and (4) Congress seems unwilling or unable to establish priorities in this bonanza of health and medical care programs. The great (and sometime philosopher) Mae West was correct in saying, "Too much of a good thing is never quite enough."

Enormity of Problem

Let me give you some idea of the enormity of the problem which must be solved. National health expeditures reached a total of $118.5 billion in fiscal year 1975, an increase of almost 14% over the previous year—in the past 20 years, expeditures increased an *average* of *more than 12% a year.* Health expenditures accounted for 8.3% of the G.N.P. in 1975 (it was 7.2% in 1970 and is estimated to be 10% if unchecked in ten years). The federal government spends 11.3% of its budget for health.

Only about one-third of all payments for medical services come directly out of the patient's pocket—he pays the rest through higher taxes, higher health insurance premiums, and higher costs for goods and service. More than 80% of health insurance premiums are paid through job-related programs.

Stake of Industry

Industry, therefore, has a a big stake in the cost of health care. General Motors, for example, in 1976 will pay $825 million for its hospital, prescription drug and dental expense coverage for its employees, retirees, and their families or $1700/year for every employee. GM's health costs *increased* $123 million a year beginning in October, '75, the largest increase in their history —and *only $15 million* of the 123 million represented *increased* benefits. The rest of the increase resulted from *increased utilization and higher prices*. Put another way, health care costs now average $175 per vehicle produced by GM and $119 per vehicle produced by Ford compared to $22 a decade ago. These figures seem staggering and are indeed sobering when we realize that two huge potentially expensive federal programs—PSRO & Planning—are underfunded and in their infancy.

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*Speech given before the House of Delegates on May 19, 1976 in Rochester, during Annual Meeting of Minnesota State Medical Association.

Possible Solutions

What are possible solutions to put "a cap on" or slow the escalation of health care costs other than increased legislative controls and regulations?

First—it seems reasonable to give present programs a chance to become fully operative. Perhaps, the National Health Planning and Development Act when fully implemented will prevent costly unwarranted duplication of services and costly equipment, close down expensive misused, underused, or empty hospital beds, and promote and encourage outpatient surgery where indicated. The PSRO program must be adequately funded to determine whether this legislation will increase quality of medical care as well as reduce costs by utilization and peer review as we were assured by the proponents of this legislation. Dr. Ted Cooper, Assistant Secretary for Health at HEW, has made a strong case for this concept of "no new programs until those on the books are evaluated."

Second—responsible leaders of labor, industry, and the insurance industry must implement changes in health insurance coverage to do away with first dollar coverage and reinstitute the concepts of deductibles and co-insurance so that the individual is aware of and has a stake in the cost and payment for medical care. Incentives should be given for outpatient coverage to relieve the current pressures for hospitalization.

Third—a strong argument can be made to increase emphasis on programs of health education and preventive medicine—not the annual checkup and periodic examination push—but rather to emphasize and teach the importance of social and economic problems that impact significantly on total health care such as housing, sanitation, education, accident prevention, smoking and alcoholism, and environmental and industrial pollution.

Fourth—an attack on the funding for basic research, unless it relates directly to health care, has been popularized recently by Senator Kennedy. A new look at the concept of categorical grants for cancer, arthritis, and heart disease is being urged. Are appropriations of large sums of money the way to conquer these diseases? Someone must determine national health priorities and what share of the total expended for health care should be spent on end-stage renal disease, heart transplants, coronary bypass surgery, joint replacement and, for that matter, each of the new and developing technologies.

Fifth—several major pieces of federal legislation including NHI proposals have called for a National Health Council to establish priorities, direction, and goals for a national health policy. This is very attractive, but only if such a council could be above and beyond control of the politicians, lobbies, and pressure groups.

National Health Insurance

I don't expect that adoption of these proposals or others will determine whether National Health Insurance will be enacted. I believe it will be, as soon as there is a concensus on how NHI will be financed. If the escalation of health care costs is not controlled by that time, NHI legislation will certainly incorporate strict regulation of medical care fees and services. By not having already accepted the leadership role in resolving the problem of health care costs, we may even now be too late.

I leave you with this statement made by Dr. Charles H. Mayo on August 9, *1919:* "The government has dabbled in medical affairs at enormous expense for what has been accomplished." If that statement were true in 1919, it has become even more evident in the past decade. Government must accept full responsibility for a large share of the escalation of health care costs but we must be in the forefront in seeking solutions to the problems of cost containment.

I am grateful for this year as your President—

I have enjoyed it thoroughly—and to be perfectly honest, I am sorry it is ending. I want to thank all of you who have been kind, helpful, and supportive of my efforts.

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Request for Physician's Art Work

For many years the Board of Editors of Minnesota Medicine has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers have received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Pictures will be returned if identified with the name and address of the physician. Please submit your picture as prospective cover subjects to the Editor of Minnesota Medicine, 101 East 5th St., Suite 900, St. Paul, Minnesota 55101.

During 1976 the Editors would like to pay homage to the Bicentennial by having our covers depict places, events, objects, scenes, etc., that have historical or patriotic significance for the State of Minnesota. Please keep the Bicentennial theme in mind when submitting prospective covers for 1976.

Farrell Stiegler, M.D.
Cover Editor

Southern Minnesota Medical Association

The annual meeting of the Southern Minnesota Medical Association will be held September 25, in Albert Lea. The Kahler Motel is the meeting place. Contact: Ethel A. McClane, Secretary, 1726 No. 4th St., Mankato 56001.

Minnesota State Medical Association

Annual Meeting

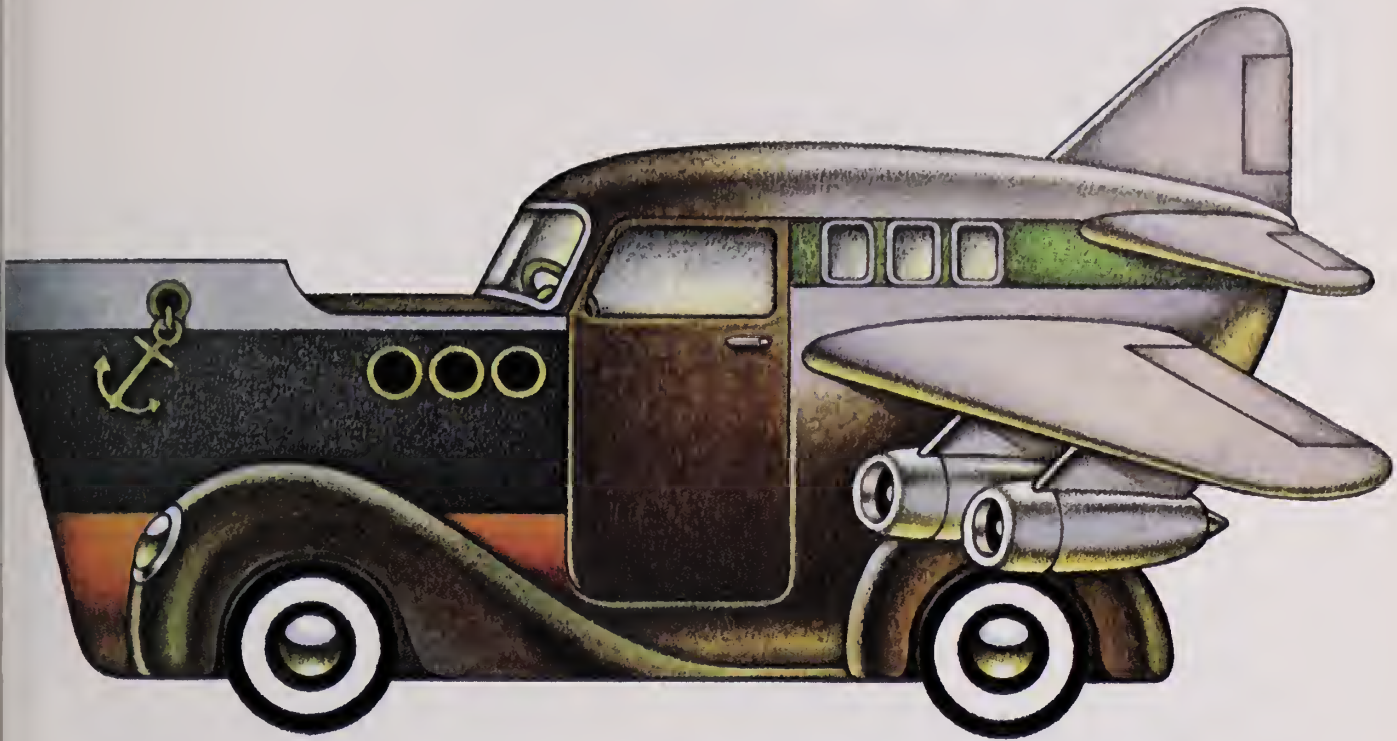
Now, what was it you wanted . . .

The Subcommittee on Scientific Assembly looks forward to an Annual Meeting that will not only be publicized as one of the best but remembered that way as well. We aim to please most of you, and we will as soon as we decipher your Meeting desires. The following is a random sampling of your comments from CME '76 evaluation cards:

Good topics—more time needed (3 days) couldn't take in everything
Continue this format
You urge members to visit exhibits but you do not allow time out of the courses to do this. Each course should have an hour free to visit exhibits each day but 'time outs' should be staggered so as not to *crowd* the exhibit space
Continue medical-political program such as session on PL 93-641
Confusing to have meetings spread out. Very poor instructions given on how to find various places.
. . . Meetings themselves were excellent. Would have been much better if things were located closer together
Should have a map of meeting locations
How about coffee and coffee breaks
Thank you! I came along whenever allowed. I'm a physician's wife and R.N. Please keep it possible. I love to learn
I think this meeting was the best of any of the State Medical Meetings that I have ever attended. I would particularly like to applaud the staff of MSMA
Scientific sessions well prepared
Don't assume as much specialist jargon as was done today—it's good to have basic explanations after fancy words
Good meeting except not enough time to visit exhibits
Continue same format of indepth program. Stress material which is practical
Good material presented—excellent talks
Difficulty finding Mayo Clinic
Request a list of preregistered physicians to be made available at meeting
Information on auto parking should be included in preliminary data
More signs on locations
Good to rotate meetings
Either drop exhibits or make it easier to visit them . . .
Time wasted finding meeting rooms
Format good, geography poor . . .
Facilities in Rochester are less than excellent. Why not have all future meetings in Minneapolis.
No time to view exhibits.
More publicity on location of registration, seminars, etc.
Distances too great for fat old physicians—exhibitors do not get treated fairly in this format

Given these suggestions, what would you do . . .

R. D. Semsch, M.D., Chairman
Scientific Assembly Subcommittee



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Usage in Pregnancy: See "Contraindications."

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This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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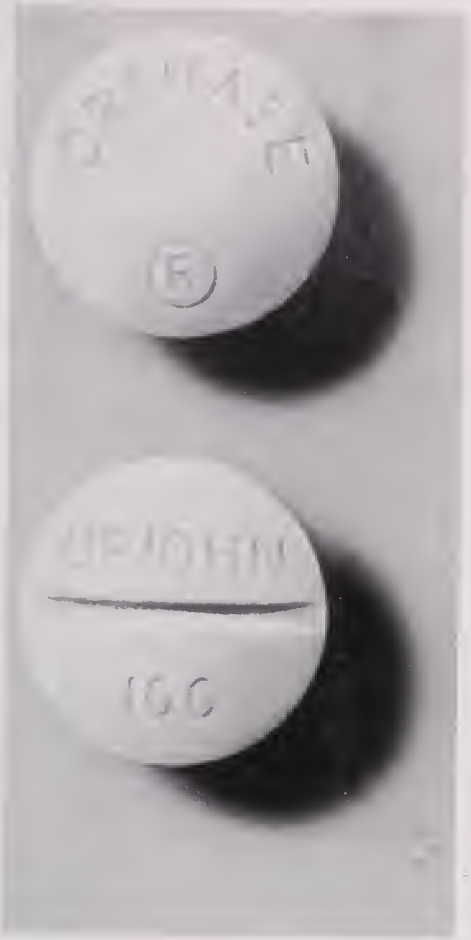
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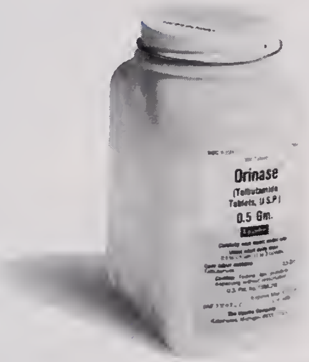
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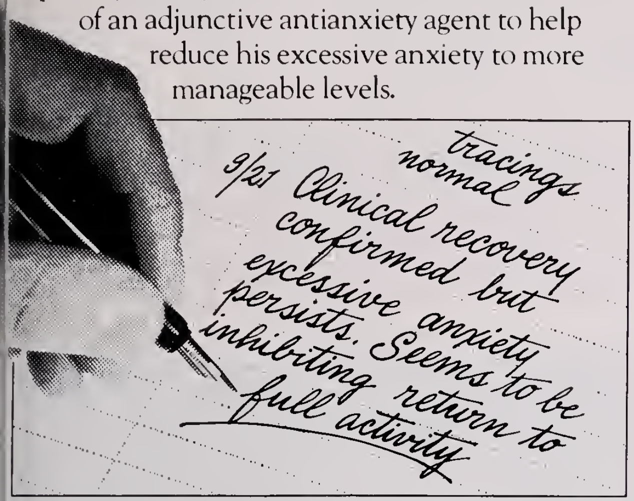
Clinical anxiety, for example, may be one reason for prolonged recuperation following cardiac healing. Yet anxiety can sometimes be beneficial in facilitating patient compliance.

The patient who is realistically concerned about resuming his precoronary functioning may be highly motivated to adhere to his rehabilitation regimen. However, the cardiac patient with *excessive* or unresolved anxiety may be so fearful of future heart failure that he refrains from your prescribed regimen. These excessively anxious cardiac patients eventually present the same clinical characteristics as patients deconditioned by bed rest.

Excessive anxiety can interfere with patient management

When excessive anxiety diminishes your

patient's ability to participate fully in his rehabilitation program, your counseling and reassurance are often sufficient. But when his anxiety is so great that it actually interferes with his ability to listen and respond, you may want to consider the addition of an adjunctive antianxiety agent to help reduce his excessive anxiety to more manageable levels.


9/21 Clinical recovery confirmed but excessive anxiety persists. Seems to be inhibiting return to full activity
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*Zohman BL. *Geriatrics* 28:110-119, Feb 1973

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Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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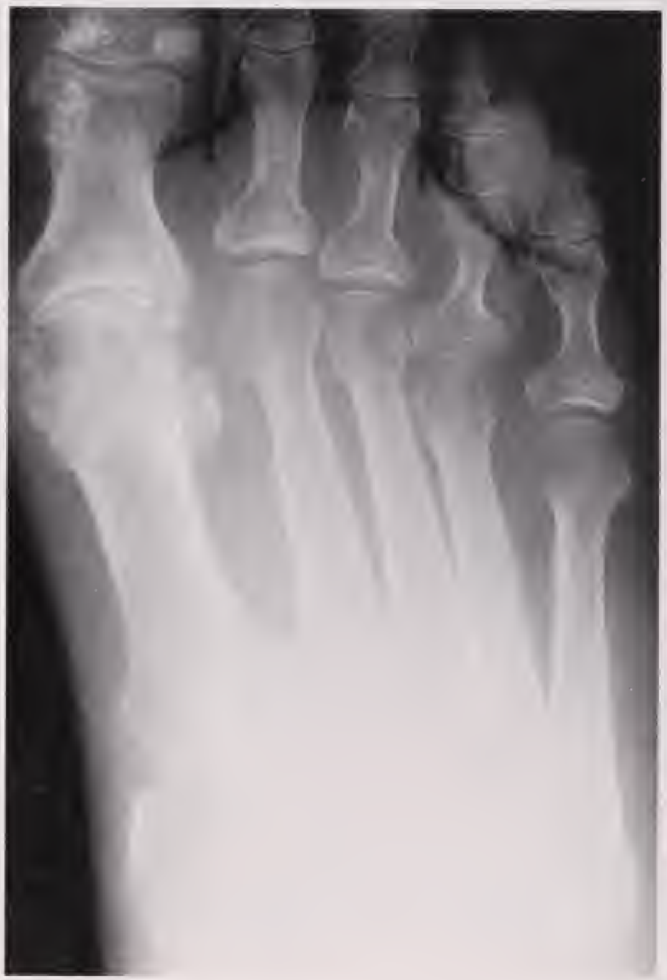
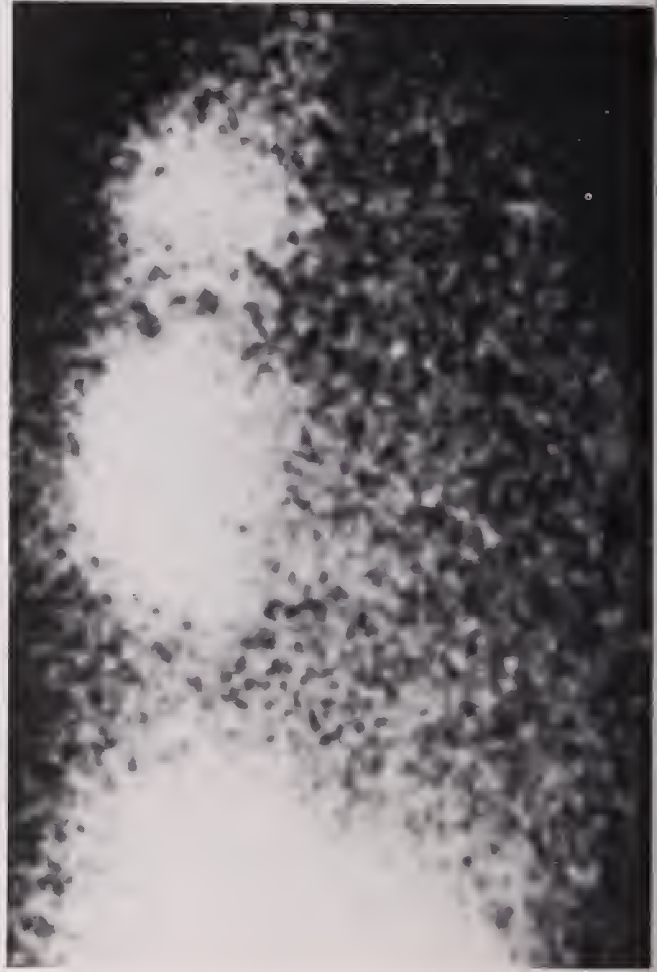


Foot of patient with acute gouty arthritis as seen by conventional x-ray.



Scintiphotogram of same foot reflects inflammatory process.

The scintiphotograph on the right shows increased uptake of radiotechnetium polyphosphate in the metatarsophalangeal joint and the proximal interphalangeal joint of the great toe of a patient with acute gouty arthritis. This increased uptake probably results from increased vascularity in the affected areas.

For a more detailed description of scintiphotography, see "addendum" at right.

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in selected patients*

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For a brief summary of prescribing information, please see following page.

addendum

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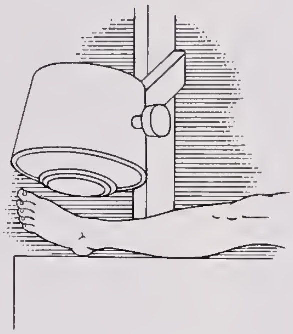
Facts about Scintiphotography



In recent years a variety of radiopharmaceuticals have been employed to aid in the diagnosis of bone and joint disorders. The joint-imaging technique consists of injecting technetium polyphosphate intravenously, and imaging is performed with the scintillation camera two hours after the administration of the radionuclide. In general, for joint surveying, the shoulders, elbows, hands, wrists, knees, ankles, feet, and vertebral column are mapped. The entire scanning process takes approximately one hour. The criterion for a positive image is a higher concentration of radioactivity in a joint region than in adjacent nonarticular bone. In effect, each patient serves as his own control.

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Contraindications: Children 14 years of age and under; pregnant women and nursing mothers; active gastrointestinal lesions or history of recurrent gastrointestinal lesions; allergy to aspirin or indomethacin.

Warnings: *Gastrointestinal Effects:* Because of the occurrence and, at times, severity of gastrointestinal reactions, be continuously alert for any sign or symptom signaling a possible gastrointestinal reaction. The risks of continuing therapy with INDOCIN in the face of such symptoms must be weighed against the possible benefits to the individual patient. Gastrointestinal effects may be reduced by giving the drug immediately after meals, with food, or with antacids. Use greater care in aging patients.

Ocular Effects: Corneal deposits and retinal disturbances, including those of the macula, have been observed in some patients on prolonged therapy. Discontinue therapy if such changes are observed. Ophthalmologic examination at periodic intervals is desirable in patients on prolonged therapy.

Central Nervous System Effects: INDOCIN may aggravate psychiatric disturbances, epilepsy, and parkinsonism, and should be used with considerable caution in patients with these conditions. If severe CNS adverse reactions develop, discontinue the drug.

Precautions: Blurred vision may be a significant symptom that warrants a thorough ophthalmologic examination. Patients should be cautioned about engaging in activities requiring mental alertness and motor coordination, as driving a car. Headache which persists despite dosage reduction requires complete cessation of the drug. May mask the usual signs and symptoms of infection; therefore, the physician must be continually on the alert for this and should use the drug with extra care in the presence of existing controlled infection. After the acute phase of the disease is under control, an attempt to reduce the daily dose should be made repeatedly until the patient is off entirely.

Drug Interactions: Although INDOCIN has not influenced the hypoprothrombinemia produced by anticoagulants, patients on anticoagulant therapy should be observed closely for alterations in prothrombin time. In patients receiving probenecid, plasma levels of indomethacin are likely to be increased and a lower total daily dose of INDOCIN may produce a therapeutic effect; increases in the dose of INDOCIN should be made cautiously and in small increments.

Adverse Reactions: *Gastrointestinal Reactions:* Single or multiple ulcerations of the esophagus, stomach, duodenum, or small intestine, including perforation and hemorrhage, with fatalities in some instances; rarely, intestinal ulceration has been associated with stenosis and obstruction; gastrointestinal bleeding without obvious ulcer formation; perforation of preexisting sigmoid lesions (diverticulum, carcinoma, etc.); rarely, increased abdominal pain in ulcerative colitis patients or development of ulcerative colitis and regional ileitis; gastritis may persist after the cessation of the drug; nausea, vomiting, anorexia, epigastric distress, abdominal pain, and diarrhea.

Eye Reactions: Corneal deposits and retinal disturbances, including those of the macula, have been observed on prolonged therapy; blurring of vision.

Hepatic Reactions: Rarely, toxic hepatitis and jaundice, including some fatal cases.

Hematologic Reactions: Aplastic anemia, hemolytic anemia, bone marrow depression, agranulocytosis, leukopenia, and thrombocytopenic purpura may occur rarely. Since some patients manifest anemia secondary to obvious or occult gastrointestinal bleeding, appropriate blood determinations are recommended.

Hypersensitivity Reactions: Acute respiratory distress, a rapid fall in blood pressure resembling a shock-like state, angioedema, dyspnea, asthma, angiitis, pruritus, urticaria, skin rashes, purpura.

Ear Reactions: Hearing disturbances—deafness reported rarely; tinnitus.

Central Nervous System Reactions: Psychic disturbances including psychotic episodes, depersonalization, depression, and mental confusion; coma; convulsions; peripheral neuropathy; drowsiness; lightheadedness; dizziness; syncope; headache.

Cardiovascular-Renal Reactions: Edema, elevation of blood pressure, hematuria.

Dermatologic Reactions: Loss of hair, erythema nodosum.

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(Continued to page 584)

MSMA Highlights

Physician's Health Forces—Let's Get Involved

The enactment by the United States Congress of Public Law 93-641 (National Health Planning and Resources Development Act of 1974) may completely restructure the health delivery system in this country. This new law is just now getting off the ground, so it is still too early for physicians in Minnesota to notice how it affects their practice.

Because P.L. 93-641 directly affects each and every physician and how he or she practices medicine, it is important for the medical profession to provide as much input as possible into the newly created health systems agency boards of which there are seven in Minnesota.

At least one portion of Minnesota P.L. 93-641 got an early start as a result of the Health Board of the Metropolitan Council. This planning Board has now been designated as a conditional Health Systems Agency for HSA 5. Because of its early beginning, physicians in the seven-county metropolitan area have had an opportunity to see the effect of this type of program on their practice. When this effect became known, physicians in the seven-county area were organized into an Advisory Committee called the Physician's Metropolitan Health Force. Catalyst for this Advisory Committee of physicians is John B. Coleman, M.D. of St. Paul.

The following is a recent interview with Dr. Coleman on how he and his colleagues in HSA 5 have worked to provide input in the consumer dominated Health Board of the Metropolitan Council.

Editors: Dr. Coleman, why do we need to change a health care delivery system that is already providing high quality care at reasonable cost?

Dr. Coleman: In the Metropolitan area, we have worked on the premise that some kind of formalized change is inevitable. The present system has many features which are excellent and must be protected, and it can only be protected by doctors getting into action, since we know more about the practicalities of medical care than anyone else, including Congress. Organized health care planning is not all that bad, but it could be without active involvement of physicians.

Editors: Is it reasonable to expect physicians in the other six HSA regions in Minnesota to form Advisory Committees such as you have established here in the metropolitan area?

Dr. Coleman: The metropolitan area may be better suited for organizing physicians since about half the population of our state and half the physicians are here and the distances are less. Nevertheless, the pattern of our efforts can be carried out in the other health service areas. The choice is to have others plan how we will practice medicine, not in some distant future—but *now*. There are only two physicians on the Health Board (HSA 5), and they have been overwhelmed by the militancy and bias of some of the consumer members. The consumers hold the power. Our Physician's Metropolitan Health Force is made up of members elected by the county medical societies within this HSA region.

Editors: From what we understand, you have gotten physicians involved in relating to the Health Board and have earned begrudging respect from this consumer dominated body.

Dr. Coleman: This is true. They are beginning to recognize we do have something to contribute and we are interested in health planning that makes sense. We want doctors on committees that have a specific purpose. Here is how it is done. When the Metropolitan Health Board sets up a special committee or task force to work on a project and to come up with a decision of policy, the Physicians Metropolitan Health Force does the same thing. A counterpart committee is formed to study the same policy or project and follow the HSA's actions. Ours is called a Reference Group. The main purpose of the Reference Group is to furnish the expert medical information or advice to the HSA. This is where the input can be most influential. When people sit down and roll up their sleeves, they become more practical and less theoretical. Decisions are the perogative of the HSA Board. Our job is to help guide those actions with facts. We have to remember that a doctor can appear just as prejudiced, unreasonable, and even ignorant to the consumer on the HSA Board as some of them may appear to us.

Editors: Can this type of physician relating really occur in the other six HSA regions in Minnesota?

Dr. Coleman: It is imperative. It is the purpose of the Minnesota State Medical Association to assist doctors in every part of the state in their dealings with HSA. MSMA is forming a new Committee on Health Planning at the state level to assist physicians.

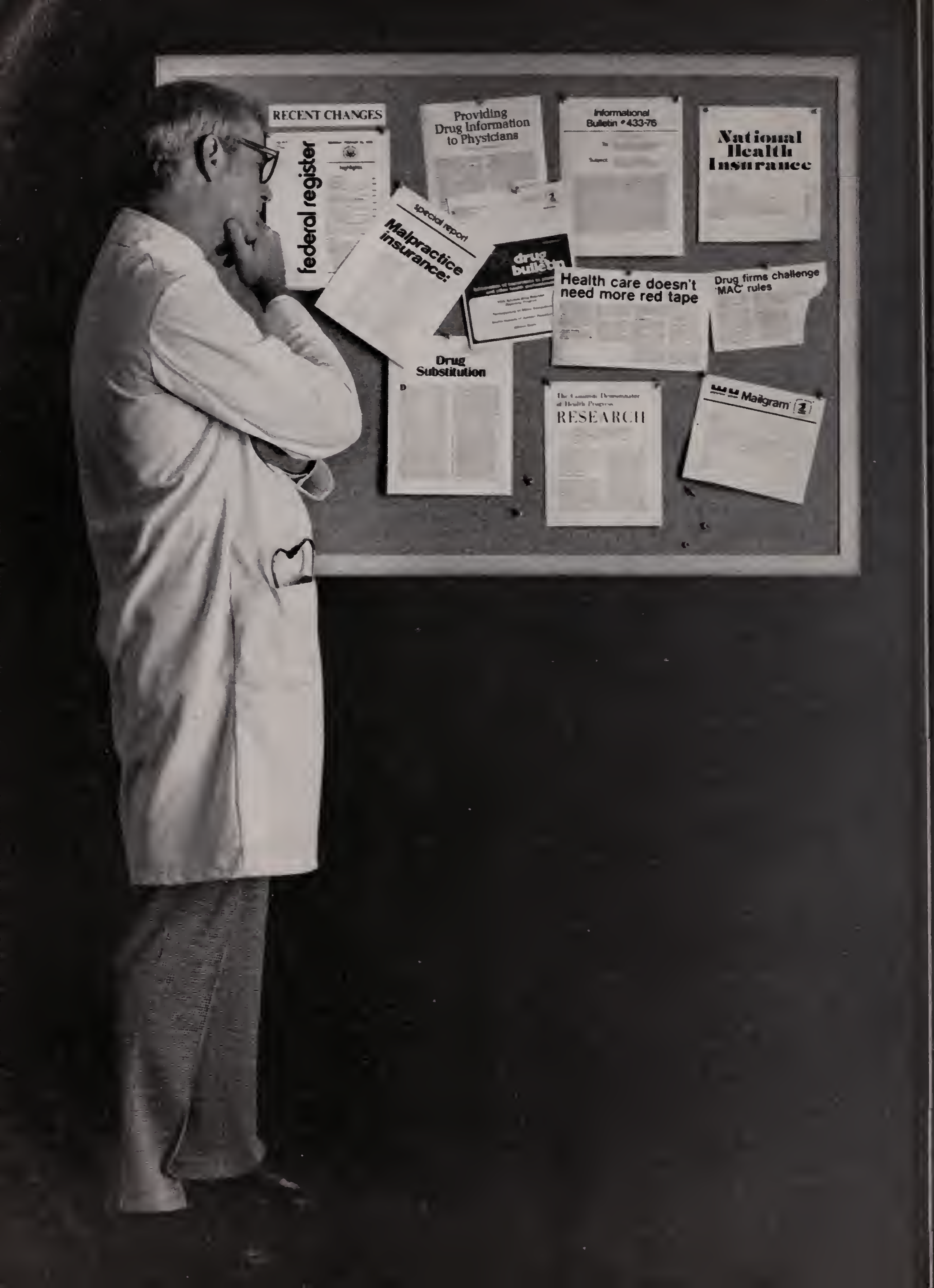
The Minnesota State Medical Association's new Division of Socio-Economic Affairs has established a Department of Health Planning to help physicians throughout the state of Minnesota to relate to the health planning process. Questions on health planning may be directed to the Director of this Department of Health Planning: Thomas Galligan at the offices of the Minnesota State Medical Association.

University of Minnesota

Continuing Education

"Current Concepts in Acid-Peptic Disease."—September 10-11 at Bethesda Lutheran Hospital, St. Paul. Program is acceptable for 9½ prescribed hours by the American Academy of Family Physicians.

Contact: Director, Continuing Medical Education, Nolte Center for Continuing Education, University of Minnesota, Minneapolis, 55455.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Medicine today is in the spotlight, subjected to all kinds of scrutiny. Your control over patient therapy is being monitored, judged and occasionally abrogated, sometimes by unknown third parties.

The worry is that in the wake of this focus, the relationship between you and your patient will be weakened, without offsetting benefits. Consider three examples:

Drug substitution In most states, pharmacy laws, regulations or professional custom stipulate that your non-generic prescriptions be filled with the precise products you prescribe. But in the last five years, a dozen or more State laws have been changed, permitting the pharmacist in most cases to select a product of the same generic drug to fill any prescription.

Ironically, this dilution of physician control has taken place against a background of growing evidence that purportedly equivalent drug products may be inequivalent, since neither present drug standards nor their enforcement are optimal. In fact, the FDA itself says it has not enforced the same standards for hundreds of "follow-on" products that it had applied to the original NDA approvals. Thus physician control over patient therapy is being eroded with a risk that patients may be exposed to drugs of uncertain quality.

The major advertised claim for substitution is reduced prescription prices for consumers. Yet no documentation of any significant savings has been produced.

MAC Maximum Allowable Cost, MAC for short, is a Federal regulation designed to cut the Government's drug bill by setting price ceilings for drugs dispensed to Medicare and Medicaid patients. Unless the prescriber certifies on the prescription that a particular product is medically necessary, the Government intends to pay only for the cost of the lowest-priced, purportedly-equivalent, generally-available product. The effect of the program may be that elderly and indigent patients will be restricted to products which someone in Washington believes are priced right. Practicing doctors will have little to say about administration of the program, since Government will have absolute authority to make its choices stick.

The drug lag The future of drug and device research depends upon a scientific and regulatory environment that encourages therapeutic innovations. The American pharmaceutical industry annually is spending more than $1 billion of its own funds and evaluating more than 1,200 investigational compounds in clinical research. Disease targets include cancer, atherosclerosis, viruses and central nervous system disorders, among others. But there is a major barrier to the flow of new drugs to your patients: The cost of the research is more than ten times what it was, per product, in 1962; and whereas governmental clearance of new drug applications took six months then, it commonly consumes two years now.

The FDA needs adequate time, of course, to consider data. But it is equally clear that the present approval process contributes to needless delay of needed therapy. That's why the increased efficiency of the drug approval process is vital to all our futures.

If these issues concern you, we suggest that you make your voice heard—among your colleagues and your representatives in State legislatures and in Washington.

It could make a difference in your practice tomorrow.

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Pediatrics

A Look at Child Health Manpower in Minnesota

Distribution and Context within the Health Planning Regions

STEVEN G. THOMPSON;* ROBERT W. TEN BENSEL, M.D.* and EILEEN A. CROWLEY

The distribution of health professionals—pediatricians, pediatric nurse practitioners, and family practitioners, who are delivering primary care to children and their families in Minnesota is examined.

RECENT REPORTS in the state of Minnesota by the Health Subcommittee of the Minnesota Senate Health, Welfare and Corrections Committee (January, 1974)[1] and by the Metropolitan Health Board of the Metropolitan Council (February, 1974)[2] echo a concern for the right of Minnesota citizens to access to acceptable comprehensive health care services. Yet while commitment of all groups to improve the health care situation in the state is strong, lack of specific information on various health services throughout the state is an obstacle to improvement.

The purpose of this report is to provide data on the distribution of specialized Pediatric health care personnel in Minnesota. In the course of compiling this research, related data on populations and economic status of the Minnesota Health Planning Regions, and on the distribution of physicians and registered nurses in outstate Regions, was also obtained. When the results of our study of Pediatric personnel are viewed in relation to what we have called the context of other health services in the state, we find a confirmation of what a number of other investigators have maintained—that existing patterns of health care distribution are a result of considerations other than need.

A final word on the limitations of the present study is necessary. The focus of this study is on the distribution of specialized child health personnel—Pediatricians, physicians in the specialties and in research who meet certain criteria, and Pediatric Nurse Practitioners. A considerable per-

TABLE 1
Distribution of Primary Care Pediatricians and Other Child Health Manpower by Minnesota Health Planning Regions

Region	1972 Estimated Population (0-18)*	Physicians† I	II	III	IV	Ratio: I/Pop. (0-18)
Northwest	54,102	1				1/54,102
Northeast	123,176	8			1	1/15,397
West Central	64,171	11				1/ 5,834
Central	142,680	7				1/20,383
Southwest	105,313	12				1/ 8,776
South Central	75,850	7				1/10,836
Southeast	141,196	23		31	1	1/ 6,139
Metropolitan	709,652	105	9	76	29	1/ 7,659
Minnesota Total	1,416,140	174	9	107	31	1/ 8,139

*Minnesota regional population estimates from Minnesota Department of Health, Section of Vital Statistics.

†Key to Physician Activity.

I Pediatricians delivering primary care to children (50% or more time).

II Family Practitioners or General Practitioners holding membership in a Pediatrics professional society.

III Physicians involved in research and specialists; (i.e., Urology, Hematology, Neurology, Psychiatry) holding membership in a Pediatrics professional society.

IV Pediatricians in administrative or teaching capacities whose practice is not at least 50% time devoted to the delivery of primary care to children.

This project was funded on Grant Number 1 D10 NU 00586-01, Department of Health, Education and Welfare.

*School of Public Health, Pediatric Nurse Associate Program, University of Minnesota, Minneapolis.

centage of child health services, especially in outstate Regions, is performed by Family Physicians and General Practitioners. Much valuable research in the area of Family Practice has been done by John W. McConnell, M.D., Department of Family Practice and Community Health, University of Minnesota.

Method

We first obtained the membership lists of the three Pediatric professional societies having members in Minnesota: The American Academy of Pediatrics, the Northwest Pediatrics Society, and the Twin Cities Pediatrics Society. These lists were then collated for duplication of membership and compared with available hospital and medical school staff lists as a check on possible omissions. Through telephone and personal contacts with physicians, administrators, and officials throughout the state, we were able to update our list as of September, 1974 and to assign to appropriate categories the current activities of the physicians (see Table 1, note 2).

We were advised by physicians and officials in various Regions that significant numbers of Minnesota residents living near state boundaries utilized child health services in bordering states. Four such out-of-state locations were identified and are included in the results.

To determine the distribution of Pediatric physician manpower in the state, we assigned the physicians in all categories to the Minnesota Health Planning Region in which they were located. We then obtained the estimated child (0-18 years) populations as of 1972[3] (the most recent estimates available) for each region and computed the ratios of primary care Pediatricians to child population for each Region (Table 1).

Finally we compiled a list of Pediatric Nurse Practitioners employed in the state through contacts with administrators of the training programs for these specialists at the Mayo Clinic and the University of Minnesota (Table 3).

Discussion

The method employed in collecting the above data was clearly inadequate for a comprehensive tally of Family Practitioners and General Practitioners delivering primary care to children or of physicians in the specialties and in research in the field of Pediatrics. We feel, however, that the present study did yield an accurate picture of the distribution of primary care Pediatricians, administrative and teaching personnel in Pediatrics, and Pediatric Nurse Practitioners practicing in Minnesota.

It should be pointed out that the statistical ratios of primary care Pediatricians to child popu-

TABLE 2
Child Health Physician Manpower in Minnesota by Location

Region	Location	I	II	III	IV
Northwest	Crookston	1			
Northeast	Duluth	6			1
	Virginia	2			
West Central	Fargo, N.D.*	11			
Central	Brainard	1			
	St. Cloud	6			
Southwest	Redwood Falls	1			
	Sioux Falls, S.D.*	5			
	Watertown, S.D.*	2			
	Willmar	2			
	Worthington	2			
South Central	Mankato	6			
	St. Peter	1			
Southeast	Albert Lea	2			
	Austin	2			
	Faribault				1
	LaCrosse, Wisc.*	8		1	
	Red Wing	2			
	Rochester	6		30	
	Winona	3			
Metropolitan	Anoka		1		
	Burnsville	1			
	Coon Rapids	2			
	Minneapolis	51	1	56	23
	Minneapolis Suburbs	14		8	1
	St. Paul	37	2	12	5
	Stillwater		5		
Minnesota Total		174	9	107	31

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*These locations are listed and included in Minnesota total because many Minnesota residents utilize the Pediatric services available there as the closest to their place of residence.

TABLE 3
Employed Pediatric Nurse Practitioners in Minnesota

Region	Location	PNPs
Northeast	Virginia	1
	Grand Rapids	1
South Central	Alden	1
Southeast	Rochester	4
	Red Wing	1
Metropolitan	Minneapolis	19
	St. Paul	5
	Fridley	2
	St. Louis Park	2
	Lakeville (Dakota Co.)	1
	New Brighton	1
	Wayzata	1
Minnesota Total		39

lations (Table 1) for the Regions can be deceptive when geographic factors are not taken into account. This consideration is especially significant in the case of the data for the West Central Health Planning Region where all of the Pediatricians are in practice in a single location, Fargo, North Dakota (Table 2).

It is clear from this overview of the distribution of specialized child health personnel in the state that serious inequalities in the availability of child health services exist in the different areas of the state. The inequitable distribution of health services in Minnesota, however, is not restricted to child health specialists. A brief look at two of the indicators of the total health care situation can provide a context within which the status of child health care can be seen as part of a broader pattern of inequitable distribution of other health services in the state.

The Regional distribution of all primary care physicians in outstate Minnesota mirrors the pattern already seen for Pediatricians. All the Minnesota Regions which were in the lower half of the state in terms of potential child patient to Pediatrician ratio are also in the lower half of the state in terms of total population to primary care physician ratio (with the exception of the West Central Region where the former ratio is skewed by the large concentration of Pediatricians practicing in a single location). Although data for the Metropolitan Region was not available, we again see that the Southeast Region, containing Olmsted County and the Mayo facilities at Rochester, has the best total population to physician ratio of the Regions for which data is available (Table 4).

This distribution pattern also exists for employed registered nurses. Again we find the Southeast Region (Olmsted County—Rochester) at the top of the list in terms of the ratio of registered nurses to total population and the Northwest and West Central Regions at the bottom (Table 5).

TABLE 5

Distribution of Employed RNs in Minnesota by Region*

Region	Employed RNs	RNs/1972 Population
Northwest	446	1/338
Northeast	1421	1/243
West Central	609	1/302
Central	1310	1/282
Southwest	1052	1/279
South Central	912	1/242
Southeast	2152	1/181

*1973 Data from A Technical Report of Health Manpower, Minnesota State Planning Agency, Comprehensive Health Planning.

The consistency of the pattern of distribution of health care personnel throughout the state tends to reinforce the conclusion that under-representation of any particular category of health care professional in a given region is not accidental. It seems clear that demographic, economic, and cultural characteristics of certain regions have a serious impact on the decisions of qualified health professionals with respect to settlement.

Conclusion

The problem of inequitable distribution of health care services in Minnesota cannot be seen as solely the responsibility of the health care professions. The factors which contribute to the health care situation described in this report are complex and varied. As we have seen, under-representation of one group of health care professionals (in our case, Pediatricians and Pediatric Nurse Practitioners) in a given area of the state is invariably tied to a broader pattern of inequitable distribution existing for other health services.

While the problem may begin with an overall shortage of certain types of health care profes-

TABLE 4

Distribution of Primary and Secondary Care Physicians by Region*

Region	Primary Care† Physicians	Secondary Care Physicians	Ratio: Primary Care Physicians/Population
Northwest	55	27	1/2,737
Northeast	148	156	1/2,331
West Central	63	30	1/2,922
Central	153	81	1/2,413
Southwest	133	38	1/2,209
South Central	98	49	1/2,252
Southeast	279‡	390	1/1,396

*1973 Data from A Technical Report on Health Manpower, Minnesota State Planning Agency, Comprehensive Health Planning.

†Primary Care Physicians include M.D., D.O., P.D., I.M. Secondary Care Physicians include all other specialists.

‡Approximately half of this figure are affiliated with Mayo Clinic.

sionals, Family Physicians or Pediatricians for example, the situation is seriously aggravated when the personnel which are available are inequitably distributed throughout the state. Of the many factors which are responsible for such inequitable distribution, we have suggested population density, economic status of potential patient populations, and cultural, economic, educational and professional resources of a given region as most important in determining health service availability. Those areas of the state which are, or are perceived to be, deficient in terms of one or more of the above criteria will attract fewer health care professionals than areas which are not.

This observation, supported by our findings, is largely a confirmation of similar conclusions reached by many others who have taken the broader view of the health care situation in Minnesota. By providing current data on the distribution of child health care personnel in the state, we hope to contribute to an initial step toward a solution to the problem of inequitable health care service distribution. Because of the acknowledged importance of child health supervision and early diagnosis of developmental irregularities, we believe the problem of inequitable distribution of Pediatric services in the state warrants a high priority in any efforts to improve the quality of health care in Minnesota.

Copies of the complete study upon which this summary is based are available upon request from the School of Public Health, Pediatric Nurse Associate Program, University of Minnesota.

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FARMFEST 76 585
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Flint Laboratories 548, 549, 550
Kjell Bergh's Borton Leasing, Inc. 514B
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Pharmaceutical Mfrs. Assn. 578, 579
Roche Laboratories .... Cover 2, 507, 570, 571, Covers 3-4
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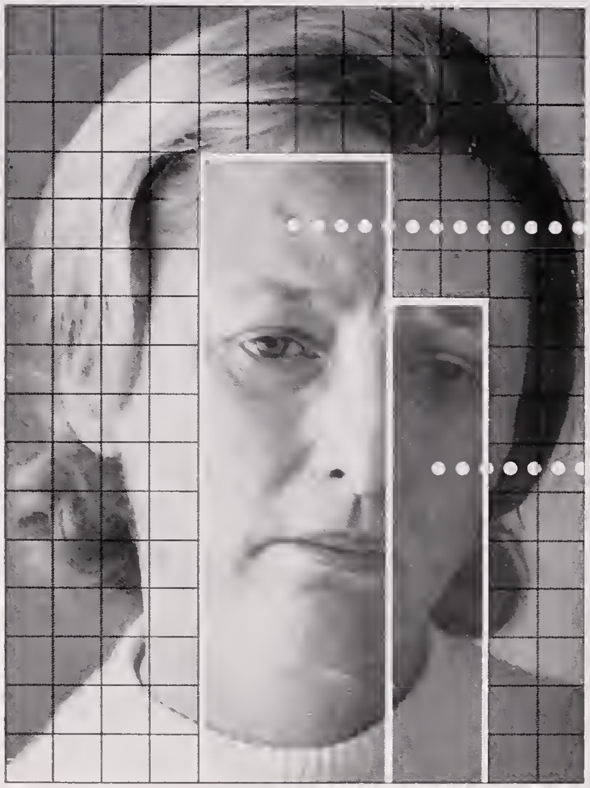
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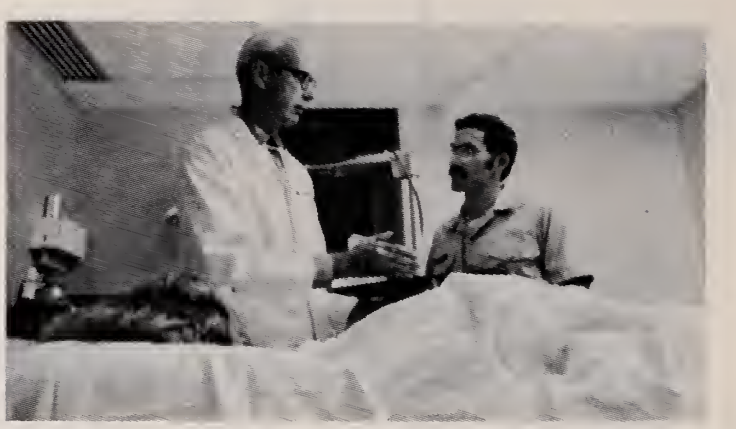

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President's Letter

Professional Liability

The physicians in Minnesota, like their colleagues throughout the country, are facing a professional liability crisis that literally threatens their ability to stay in practice—and in all instances—places a heavy financial burden on our patients who must ultimately pay for the escalating premium cost imposed on physicians and hospitals. If there is one topic on the socioeconomic agenda that will solidify the medical profession to move toward a proper course of problem solving and corrective action, it should be the national professional liability crisis.

Fortunately for Minnesota physicians there is no crisis at the present. Insurance is available and affordable. Minnesota's statue of limitations of two years compares favorably with most other states. Before seeking remedial action the Minnesota State Medical Association has stopped temporarily to look at studies of completed or closed claims specifically the Colorado Medical Society Study of 386 closed claims in 1975, the recent National Association of Insurance Commission's completed study, and our own closed claim experience with the St. Paul Fire and Marine Insurance Company.

There are three general categories, or one may call them omissions on the part of our profession that need correction. First, the failure to recognize that some alleged malpractice is indeed just that—many cases according to the Colorado Study represent good care, but deficiencies in the medical record prevented the defendant from proving it.

Secondly, is the failure to collect sufficient data to define the causes of the malpractice crisis. This has allowed half truths, paranoia, self-idealism, and innuendo to serve as a basis for corrective action rather than hard, cold facts. There is widespread belief that the leading causes of the crisis are avarice, an angry public, corrupt attorneys, contingency fees, sympathetic juries, and a Marcus Welby complex, which perpetrates the image of the all-knowing, infallible doctor. If we look in the mirror we may see that instead of a wrongful, negligent act it was really our doctor-patient relationship which created hurt feelings as abruptness, hostility, rudeness, excessive waiting, inadequate explanations and large fees are predominant causes of medical malpractice litigation. Thirdly, solutions were attempted by legislation before sufficient data were available to be secure in knowing what solutions were needed. Before others have assimilated and digested the data, they ask government to correct their grievances.

What has happened to date? Physicians have been diverse in their own corrective action depending on their states' individual problems. Some have "gone bare," others have joined the military, Veterans Administration, or a public health service. Some have moved, retired early, countersued, or limited the spectrum of their services to a low risk category. Others have joined an HMO, or larger clinic that pays malpractice premiums. Collectively where state medical associations have been confronted with loss of insurance coverage they have formed captive self insurance companies and asked their state legislatures to enact legislation for joint underwriting associations. Others have set up voluntary binding arbitration panels and others mandatory pre-screening panels. Most states have sought various types of tort liability remedial legislation.

If we add all the aforementioned up it seems like a chaotic and fragmented approach to say the least. We, in Minnesota, do have some time to witness what is happening in other states where legislation has been enacted. Hopefully, the Minnesota State Medical Association will be able to make some definite determinations as to what works and what doesn't.

The last legislature did enact a number of amendments to the medical practice act ostensibly to strengthen the hand of the Medical Board of Examiners in improving medical discipline as it relates to professional liability. Reporting of awards, handling of complaints, overview of hospital staff privileges, and changes and authorization for continued medical education (which we already have) as a condition for re-licensure were among some of the changes but, when one looks at the hard cold facts, this approach is misdirected. It is not the poorly trained, foreign trained, newly practicing doctors who are being sued. The high risk board certified specialist practicing primarily in a hospital setting and known to carry liability insurance with high limits has the majority of malpractice suits. In addition, a large number of patients are emergency room patients assigned to a physician where free choice is not available. The St. Paul Companies rarely is called on to defend the nice little guy who has his office above the drug store and apparently has remained "the patient's friend."

The State Medical Association is most concerned about what will produce a cost benefit for physician and patient and therefore, will have introduced during the next [legislative] session legislation addressing itself to periodic payments or revisionary trust funds, the collateral source rule, notice of intention to sue, informed consent, standard of care locality rule, and awarding of court costs for frivolous suits. This remedial tort legislation may or may not be the answer. What is important, however, is that the bar association, hospital association, other professions such as teachers, dentists, etc. and product manufacturers who have similar malpractice problems band together to force an equitable solution.

In addition, we as physicians should direct our energies towards our own profession with some of the following solutions:

1. Continue our efforts to strengthen the Board of Medical Examiner's authority in the area of disciplinary matters. The State Medical Association does not have the statutory authority to police their own profession. The public, quite properly, holds the profession responsible for its errant members but, we must demand and have the authority necessary to fulfill this responsibility.
2. Behavioral modification on the part of physicians in essence "what brings us to court."
   - A. Encourage patient advocacy systems.
   - B. Establish a more documented informed consent.
   - C. Improve record keeping by physicians.
   - D. Eliminate technical errors.
   - E. Eliminate systems failure within a hospital environment. i.e. an interpreted electrocardiogram or serum potassium absent from the chart prior to surgery.
   - F. Overhaul emergency room documentation of instructions. i.e. the huge trauma type case rarely developes into a suit, but the patient sent home with abdominal pain and instructions to return is.
   - G. Improved medical judgment and knowledge.

Finally Minnesota State Medical Association should put together a comprehensive, educational package including pamphlets, films, and slides that should be shown to medical groups—which would encourage physicians to do what is necessary in their own practices to reduce the risk of malpractice claims. Unfortunately, the ultimate loser in this mess is the individual consumer, our patient.

R E Anonsen

Richard E. Anonsen, M.D.
President
Minnesota State Medical Association

"Doctors' Office Call"—MSMA Annual Meeting
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Editor's Notebook

Health Care 1976, Medicine in Transition—Part II

"Change is in the Air"

Trends Affecting the U.S. Health System.
Prepared by Cambridge Research Institute October 1975.

Now that I am back in Minnesota after a six week Health Systems Management course at the Harvard Business School, my fellow physicians are asking, "What did you learn?"

I have interpreted this to mean: "Did you learn anything useful?"

Mood Towards Medicine

I think so. I learned something about the mood of the country towards Medicine. The mood is grim, determined, and even desperate.

The mood is: society can no longer tolerate escalating health care costs, and the government (or someone else) is going to have to do something about it. This mood is particularly intense in the Northeast, where the recession has hit harder than most parts of the country, and in Washington, where politicians smell the opportunity for building a larger constituency.

Change in Air

Because of this mood, change is in the air. Not the radical changes you fear, *viz*, completely abolishing fee-for-service and involuntarily herding physicians into prepaid groups. But more subtle changes, designed to control costs, to diminish physician influence, and to shift emphasis from hospital to outpatient medicine (Figure).

Problem	How Society Has Reacted	How Reactions are Changing Medicine
Escalating Health Costs (Two to three times the inflation rate of the rest of the economy for the last 10 years)	1. More government regulation: Certificate of Need, Health Service Areas (HSA's), and PRSO's.	1. Slowed rate of technological change.
	2. More cost controls by health insurers.	2. Reduced physician power and more power for hospital administrators.
	3. More insurance coverage for ambulatory and extended care.	3. Increased mergers and shared services between health care institutions.
	4. Growth of HMO's.	4. More emphasis on outpatient and extended care.
	5. Trend towards group practices.	5. Trend towards institutional rather than physician referrals.
	6. More physicians' assistants.	

Figure—Changes in the U.S. Health System. Modified and simplified from *Trends Affecting the U.S. Health System*, Cambridge Research Institute, October, 1975.

Compromises

These changes may not be to our liking, but many are occurring and are in place. Many observers, for example, believe Public Law 93-641, the National Health Planning and Resources Development Act of 1974 that set up Health Service Areas and Agencies, is the framework for National Health Insurance. My own feeling is that the fundamental political compromises in the Health Field have been made, and the following processes set in motion: a controlled and downplayed fee-for-service system, supported and promoted HMOs and other prepaid plans, and regulated and deemphasized acute hospital care with a shift of emphasis to outpatient workups and care. Despite the government's planners' talk about "preventive medicine," I am not impressed they understand what that lofty concept actually means or have any effective plan to prevent diseases.

Misgivings

Many of us at the Harvard course had deep misgivings about the government's ability to perform, i.e., to provide better health services at a lower cost. Indeed, under central government control, American citizens may have poorer services at a higher cost, or lesser services at controlled costs. Still I am convinced Medicine is in transition from doing what it wants to do to what society wants it to do.

Modifying the Change

Medicine can modify the transition by continuing to speak out on the issues, particularly when politicians bog down into ill defined rhetoric. Much of the current government talk about *quality control* is just that—rhetoric. The emphasis really is on *control*—not *quality*. The word *quality*—a noble but fuzzy abstraction in health matters—is rarely precisely defined and is often an euphemistic and semantic mechanism for introducing regulations. An effective mechanism, too, for who can object to *quality?*

I would prefer for our public officials to talk about *quality results* and am happy to see physicians are taking steps to define what quality results are.[1] *Results* are concrete and can be measured. But most government efforts, such as in PSROs, are concerned with *procedures*—the way one does things, rather than results.

Challenging Critic's Arguments

I would also like to see physicians challenge critic's assertions about too much surgery and too much technology. I have had my own go at countering the unnecessary surgery charges.[2] Physicians, I believe, are perfectly capable of developing carefully reasoned, documented, cost effective arguments of their own to defend the procedures and tests they perform.

Role of Minnesota Medicine

And perhaps Minnesota Medicine has a role during Medicine's transition phase. As Medicine changes, so should its publications. Perhaps we can inform you better what's going on in the U.S. Health System. Maybe we can give you a more balanced blend of scientific, technical, economic, and political views. I don't think straight scientific and clinical reporting—though essential—are enough to hold readers or are this Journal's sole responsibility.

Physicians need to know more about the health system as a whole. A system, by the way, may be defined as something where if you shove in one side, it bulges out the other. I'm suggesting we talk a little more about the bulges.

Richard L Reece MD

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Book Report

FINALLY . . . I'M A DOCTOR by Neil Shulman, M.D. Charles Scribner and Sons, N.Y. 1976. pp 258. $7.95.

Neil Shulman's novel of the life of a student from college years through medical school must be partly autobiographical. His description of important medical school events, the first cadaverous incision, the lecture of the pompous surgeon to the neophytes, his first encounter with a psychotic patient, are too evocative of the event to be written from imagination. He was obviously there and reporting what he saw and heard. Dr. Shulman writes for the general public but his book will interest all physicians who have lived through similar experiences. The professor should occasionally see himself through the eyes of the student. It is a leveling experience to have turgidity punctured and pomposity exposed. If this book is autobiographical one leaves it with a feeling that he would like to meet Dr. Shulman's family, his mother and his grandmother and, of course, the delectable girlfriend.

He writes well. He describes the training of the medical student to perfection. Educators should realize that some of their encounters with students will never be forgotten; to be recalled with appreciation (or condemnation) forever.

Reuben Berman, M.D.
Editor Emeritus

Laurel Wreaths

Acclaimed by the audience for its high spirited entertainment and by the Pre-School Medical Survey of Vision and Hearing and the Minnesota Society for the Prevention of Blindness for its strong financial support to their programs, the July 15 Cabaret at Orchestra Hall, Minneapolis, was a resounding success. Members of the Minnesota State Medical Association Auxiliary, particularly Mrs. William Chandler, chairman of arrangements, and Mrs. John Nilsen, her co-chairman, both of Hennepin County Medical Society chapter, deserve unstinted praise for their inspired activity in making the benefit a financial triumph. The board and staff of M.S.P.B. and the board and staff of P.S.M.S.V.H. hereby extend their hearty thanks to the members of the Auxiliary of the Minnesota State Medical Association, especially to members Mrs. William Chandler and Mrs. John Nilsen.

Robert Fink, M.D.*
and
Bourne Jerome, M.D.†

*President, Minnesota Society for the Prevention of Blindness.
†Chairman, Pre-School Medical Survey of Vision and Hearing.

Reminder: C.M.E. Reports Due

The Minnesota State Medical Association requires triennial reporting of continuing medical education credits as a condition of membership. The current requirement period will end on December 31, 1976. Send in your reports as soon as possible to keep your membership in good standing. Questions: Contact C.M.E. Dept., MSMA, 101 E. 5th St., St. Paul 55101.

Minnesota State Board of Medical Examiners

1976 Minnesota Session Laws Chapter No. 222 provides as follows:

Section 40. Minnesota Statutes 1974, Chapter 147, is amended by adding a section to read:

(147.074) (Filing of hospitals served) *Each physician shall file with the board a list of the in-patient and out-patient medical care facilities at which they have medical privileges. This list shall be updated when the physician applies for license renewal.*

This list must be submitted to the Board with your 1977 annual registration payment. Forms will be mailed to you with the annual registration renewal form.

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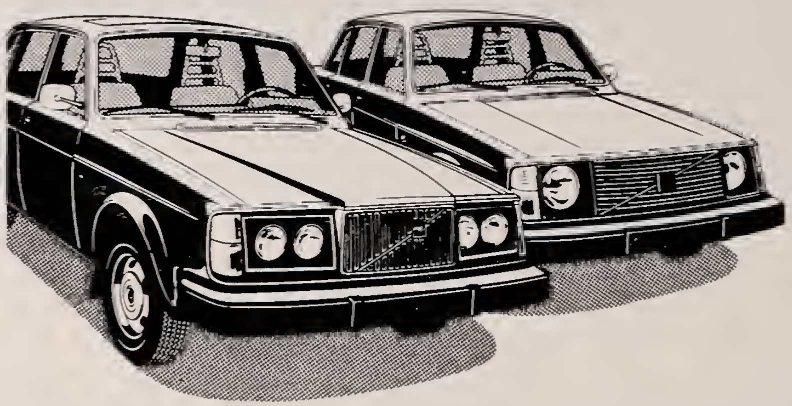

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Contents—September, 1976

OVER PHOTO—Doorways of the Medical School, University of Minnesota

RESIDENT'S LETTER—Professional Liability
Richard E. Anonsen, M.D., President 591

DITOR'S NOTEBOOK—Health Care 1976, Medicine in Transition
art II—"Change is in the Air"
Richard L. Reece, M.D., Editor-in-Chief 593

RIGINAL CONTRIBUTIONS

Barium Demonstration of Mallory-Weiss Syndrome
Donald L. Bruns, M.D. and Charles R. Nicolosi, M.D. 599

Role and Rationale of the Use of Propranolol in the Treatment of Patients with Angina Pectoris
Fredarick L. Gobel, M.D. 601

Prenatal Assessment of Intrauterine Growth Retardation
Thomas W. McDonald, M.D. and Charles R. Fish, M.D. 608

DITORIALS

Assessment of Gestational Age
Konald Prem, M.D. 623

MEDICAL COMPLIANCE—The Effect of Appointment Reminders on Keeping Appointments in a Core City Pediatric Outpatient Department
William Meller and Arnold Anderson, M.D. 625

PRESIDENT'S ADDRESS
Richard E. Anonsen, M.D. 627

SPECIAL ARTICLE—Pathology of the Myxomatous Mitral Valve
Richard B. Guthrie, M.D. and Jesse E. Edwards, M.D. 637

CORONARY—Coronary Vein Perfusion, History
Jack Kolff, M.D. and W. J. Kolff, M.D. 648

GRAND ROUNDS—Hyperlipoproteinemias—Current Concepts
Paul Koss, M.D. 655

MSMA HIGHLIGHTS—MINNPAC
Richard Engwall, M.D. 629

MINNESOTA STATE MEDICAL ASSOCIATION—Annual Meeting
R. D. Semsch, M.D. 630

BOOK REVIEWS 595, 628

CONTINUING EDUCATION 595, 618, 630, 647, 662

CLASSIFIED ADVERTISEMENTS 636

INDEX TO ADVERTISERS 662

Volume 59:9
Pages 587-662

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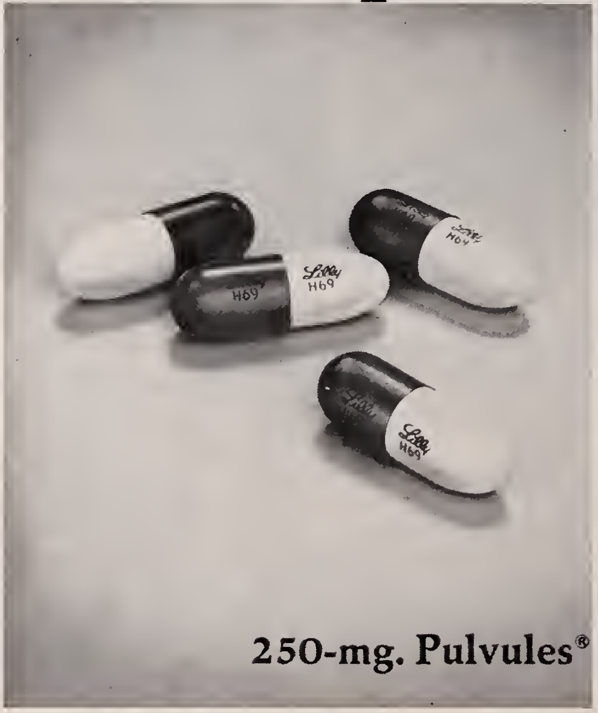

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Barium Demonstration of Mallory-Weiss Syndrome

DONALD L. BRUNS, M.D.* and CHARLES R. NICOLOSI, M.D.*

Gastroesophageal lacerations associated with hematemesis constitute the Mallory-Weiss Syndrome. The longitudinal lacerations at the cardia are rarely diagnosed by radiologic methods. A case is reported in which the tear was demonstrated by an upper GI series and confirmed by esophagogastroscopy.

ONLY SEVEN CASES of the Mallory-Weiss Syndrome diagnosed by barium studies have been reported in the English and American literature since it was first demonstrated in 1968.[1-3,9] The purpose of this paper is to document an additional case.

Case Report

A 65-year-old male was admitted on April 14, 1975, with a history of vomiting blood. He had consumed a large meal along with seven drinks the evening before admission. Following this he became nauseated and vomited partially digested food. He then vomited twice noting blood mixed with food the second time and only blood the third time. There was a past history of epigastric pain precipitated by alcohol, tobacco and spicy foods. His last barium study of the upper gastrointestinal tract in 1968 was normal.

Physical examination revealed a well developed, well nourished male in no acute distress. Blood pressure was 142/90 mm., pulse 90/min., and temperature 100.2° F. The abdomen was soft without organomegaly or tenderness. Bowel sounds were normal. The remainder of the examination was normal.

Hemoglobin on admission was 14.6 gm.% and dropped to 12.5 gm.% the following day. An emergency barium study of the upper gastrointestinal tract revealed a dissection of barium into the wall of the distal esophagus (Figure 1.) Esophagogastroscopy with the ACMI panendoscope (Model FO-7089A) disclosed a longitudinal laceration on the posterior wall of the esophagus (Figure 2) about 4.5 x 0.5 cm. in size, located at 35 cm. below the incisor teeth, and bleeding slowly. The stomach was found to be distended with blood. The stomach was emptied and the patient treated medically with hourly administrations of antacid. He recovered uneventfully.

Discussion

The Mallory-Weiss Syndrome is caused by a longitudinal tear in the esophageal wall at the esophagogastric junction. The tear usually involves the mucosa and submucosa and rarely, the muscularis.[8] These lesions are encountered most commonly, but not exclusively, in chronic alcoholics with a history of hematemesis following a bout of excessive vomiting.

Normally, a reflex relaxation of the musculature of the gastrointestinal tract precedes an antiperistaltic wave. Mallory-Weiss hypothesized that, during prolonged episodes of vomiting, this reflex relaxation fails to occur, so that reflux of gastric contents suddenly overwhelms the contraction of the cardiac sphincter, thereby producing massive dilatation and consequent tearing of the esophageal wall at the esophagogastric junction.[6]

More than 150 cases have been reported since the syndrome was first described by Mallory & Weiss in 1929.[5,7] Originally considered rare, this disorder has accounted for between 5%[4] and 15%[10] of cases of massive upper gastrointestinal bleeding.

Radiologic diagnosis of the Mallory-Weiss syndrome utilizing barium is rare. Sparberg reported the first case in 1968.[9] Review of the English and American literature from 1968 to 1975 reveals only seven such instances.[1-3,9] This paper describes an additional case. Spot films during the passage of barium demonstrated a deep tear in the wall of the esophagogastric junction posteriorly extending into the muscularis (Figure 1).

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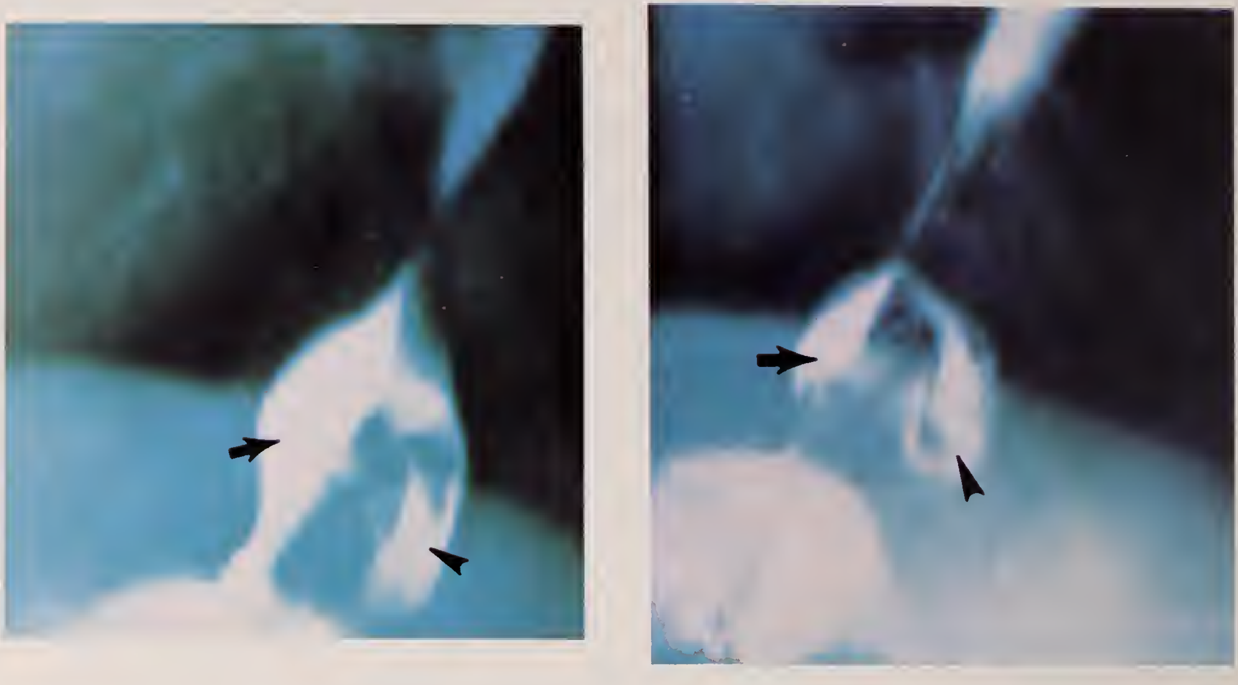

Fig. 1—The distal esophagus is seen in its relaxed (left) and contracted (right) phases. The true lumen lies anteriorly at the lesser curvature (single arrow). The dissected false channel lies posterior at the greater curvature (arrowhead). The laceration is deep and irregular with extension into the muscularis.

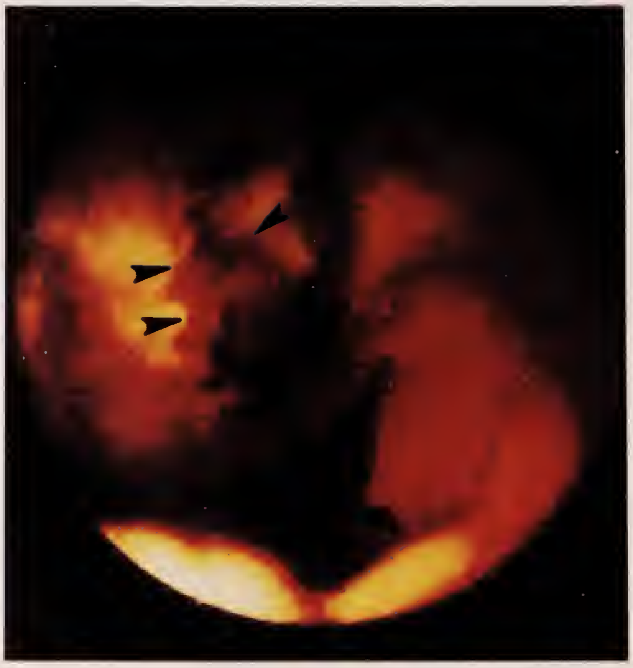

Fig. 2—An esophageal tear (arrowheads) with edematous margins and central bleeding can be seen extending down to the esophagogastric junction (single arrow).

This finding was later confirmed by endoscopy (Figure 2).

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Role and Rationale of the Use of Propranolol in the Treatment of Patients with Angina Pectoris

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In recent years propranolol has assumed an increasingly important role in the therapy of angina pectoris. Its effectiveness is achieved by reducing myocardial oxygen consumption primarily through its effect on heart rate, wall tension, and contractility.

PROPRANOLOL IS A POTENT Beta-adrenergic antagonist which has been recently approved by the Food and Drug Administration for the treatment of angina pectoris. During the past decade propranolol has been recognized as the most important drug for the treatment of angina pectoris since the introduction of nitroglycerin nearly a century ago. Other Beta-adrenergic antagonists have been found to be equal to, and some more effective than propranolol, but serious side effects have limited their clinical usefulness and propranolol is the only Beta-adrenergic blocking drug currently available in the United States. Other Beta-adrenergic blocking drugs are clinically available in Europe, and may soon be available in the United States. In light of the recent approval of the use of propranolol for the treatment of angina pectoris, concurrent with the increasing popularity of surgical treatment for angina pectoris, it seems timely to reassess the role of propranolol in such patients. This review is concerned with the rationale, as well as the pragmatic aspects of propranolol therapy for angina pectoris.

Propranolol and Myocardial Oxygen Consumption

In general, effective medical therapy of patients with angina pectoris consists of decreasing myocardial oxygen requirements during stress while effective, surgical therapy employing bypass grafting allows an increase in the blood supply to the ischemic myocardium during stress. The major determinants of myocardial oxygen consumption (MVO_2) have been identified during the past two decades and are:[1]

(1.) Myocardial wall tension (this in turn is directly proportional to the intra-ventricular pressure and to the radius of the ventricle; $T \sim Pxr$);
(2.) Myocardial contractility;
(3.) Heart rate (which has a cumulative effect on numbers one and two above);
(4.) The basal metabolic requirements of the myocardial cells;
(5.) The energy required to activate contraction; and
(6.) Coronary blood flow.

Myocardial wall tension, contractility and heart rate are, by far, the most important of these. Successful medical therapy has resulted primarily from alteration in one or more of these determinants of MVO_2. Propranolol consistently causes reductions in the exercising heart rate (HR), contractility, and blood pressure (BP).[2,3]

Propranolol in Normal Subjects

It has been demonstrated that the heart rate and the product of HR and BP correlate well with MVO_2 during upright exercise in normal subjects.[4] Alteration of these two variables by propranolol does not appear to result in a deterioration of this positive correlation.[5] In a recent study of nine normal subjects during upright bicycle exercise, (Figure 1) measurements were made of myocardial blood flow (MBF). MVO_2 and the sys-

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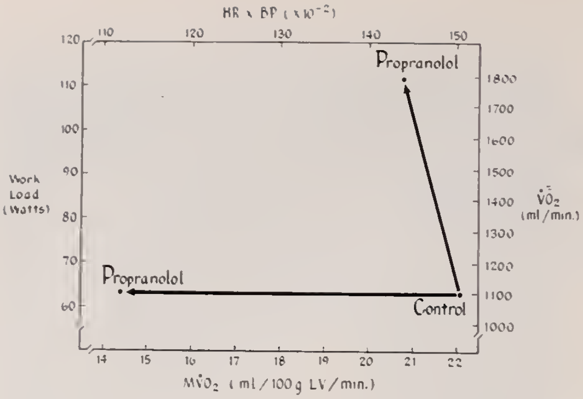

Fig. 1—Propranolol and myocardial oxygen consumption adapted from the data of Jorgensen et al.[5] Control values are indicated in the lower right hand corner of the figure and changes during propranolol therapy in the upper right hand corner (exercise level 2) and left lower corner (exercise level 3). See text for details.

tolic blood pressure during three levels of upright bicycle exercise:

(1.) Exercise sufficient to establish a "control" heart rate of 120 bts/min;

(2.) Exercise at a new external workload after propranolol (0.25 mg/Kg IV) sufficient to result in a heart rate of 120 bts/min; and

(3.) Exercise at the same external workload as in 1 after propranolol.

Results of that study indicated that during propranolol, in order to maintain a heart rate similar to control values (from exercise level 1 to 2) it was necessary to increase the external workload considerably and systemic oxygen consumption nearly doubled.[5] At the second level of exercise, MVO_2 and HR X BP remained nearly the same as the control value, indicating that nearly twice as much external work was performed at the same MVO_2. In the same respect when subjects exercised again against the same external workload as during the control period (exercise level 3), but this time during Beta-adrenergic blockade by propranolol, MVO_2 and HR X BP were considerably decreased from exercise level 1 control values. In normal subjects during upright exercise in spite of striking changes in HR and BP with propranolol the positive correlation between MVO_2 and HR X BP persisted.

Including the systolic ejection period with HR and BP as a hemodynamic predictor of MVO_2 resulted in a deterioration of the previously positive correlation. The tension time index, which is the product of the mean systolic pressure, the systolic ejection period and the heart rate did not correlate as well with MVO_2 as did the HR X BP or even HR alone.[5,6] This fits well with the experimental data which indicates that the major myocardial oxygen cost is in generating tension and not in maintaining it.[7]

This data would lead one to speculate as follows (Figure 2): In normal subjects there is a linear relationship between external work and the heart rate and between HR and MVO_2. A normal young subject can reach a heart rate in the neighborhood of 200 bts/min. If a generous dose of propranolol is given, the resting heart rate is slightly decreased at each level of external work and there is a progressively greater drop in heart rate as exercise progresses so that at maximum exercise there is a 20-30% reduction in heart rate and approximately a 40% reduction in maximal external work. In normal subjects this effect may be deleterious as it results in a reduction in maximum exercise tolerance and hence in achievable work. In patients with angina pectoris, however, chest pain usually interdicts at a heart rate well below maximum. Propranolol shifts the MVO_2—

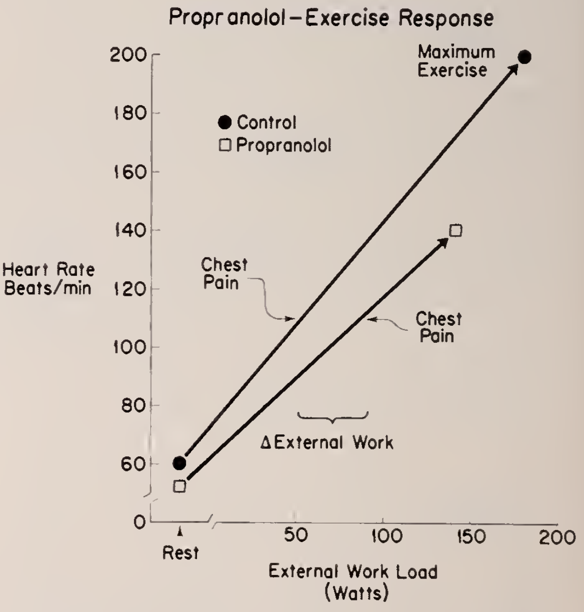

Fig. 2—Relationship between heart rate and external work in normal subjects during control (solid circles) and during propranolol (open boxes). If chest pain was to interdict at the same heart rate, as indicated by arrows, more external work could be accomplished during propranolol therapy.

external work relationship to the right and allows the subject to achieve more external work at the same heart rate, or heart rate blood pressure product, and to do the same external work at a reduction in MVO_2 or heart work. Propranolol has changed the relationship between work performed by the body (external work) and work performed by the heart.

Patients with Angina Pectoris

The general efficacy of propranolol in patients with angina pectoris is well recognized although not accepted by all.[8-14] In a recent randomized double blind study of 17 patients Alderman et al. observed a favorable clinical response in patients receiving 80 mg/day of oral propranolol but at only 160 mg and 320 mg/day dosages was statistical significance achieved.[15] These authors used a criteria of 25% or better improvement of angina frequency as being a favorable response. Thirty-five percent of patients improved at an oral dosage of 80 mg daily, 59% at 160 mg daily and 76% of patients improved at the 320 mg per day oral dose.

Extrapolation of hemodynamic findings from normal subjects to patients with ischemic heart disease and angina pectoris must be done with considerable caution, however, since changes in ventricular volume and contractility (which are two important determinants of MVO_2) are not included in commonly used indices and might be considerably greater in patients with ischemic ventricles than in exercising normal subjects. The exercising heart rate and HR X BP bears a constant relationship to the onset of chest pain in patients with angina pectoris when there is adherence to a suitable protocol.[16-18] Frishman et al., (Figure 3), noted that although patients could increase the amount of external work at the onset of chest pain by 122% during propranolol therapy the heart rate blood pressure product at the onset of chest pain was diminished by 30% from control values.[19] Other authors have also noted that the HR X BP product at symptom tolerated maximum exercise (STME) was decreased from the control values during propranolol therapy even though propranolol therapy allowed an increase in external work.[17] Thus, although propranolol allows patients with ischemic heart disease to do more external work, the HR X BP reached at the onset of chest pain (STME) is reduced.

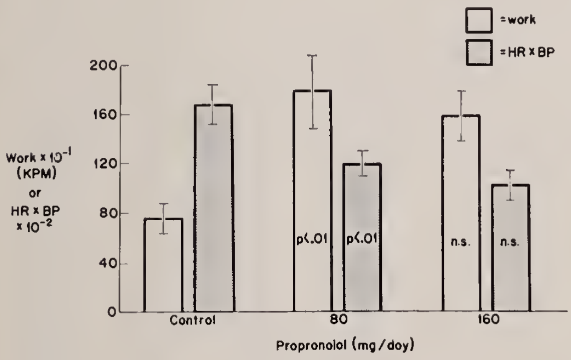

Fig. 3—The effect of propranolol on symptom tolerated maximum exercise (STME) during propranolol therapy in patients with angina pectoris adapted from Frishman et al.[19] Although external work (open bars) is increased during propranolol therapy the HR X BP product is decreased (stippled bars).

Propranolol and Ventricular Volume

These data suggest that perhaps an increase in ventricular end-diastolic volume and ventricular radius during propranolol leads to an increase in wall tension and hence MVO_2 in these patients. A recent study where ventricular volume was calculated from the internal end-diastolic diameter measured during echocardiography indicated an 11% (79 to 88 ml) increase in mean volume from control to 80 mg/day of oral propranolol and a 30% increase at 160 mg/day.[19] A decrease in ejection fraction and maximum systolic posterior wall velocity consistent with a decrease in contractility were also noted in this study.[19]

We have noted similar findings as illustrated in Figure 4 where a 30% reduction in HR X BP at STME during propranolol therapy was accompanied by a 17% increase in total heart volume as measured from an Xray gated to end-diastole. These data indicate that the reduction in the heart rate blood pressure product at STME during propranolol therapy may be related in part to an increase in ventricular volume and hence to an increase in ventricular wall tension. This in turn would result in greater myocardial oxygen requirements at the same heart rate blood pressure product. The increase in ventricular volume in turn is likely to be due to a decrease in sympathetic stimulation of the heart allowing an increase in fiber length. In patients who are dependent upon sympathetic stimulation to maintain an adequate cardiac output, blockade of that catecholamine stimulation may lead to heart failure. An increase in ventricular volume is not uniformly observed in patients receiving propranolol as indicated by a recent report where large intravenous doses of propranolol resulted in no significant change in ventricular volume or wall motion in patients with coronary artery disease.[20]

Intramyocardial Blood Flow

The effect of propranolol on the intramyocardial distribution of blood flow has not been clearly established, primarily because of the difficulty in finding a suitable experimental model. The inner subendocardial muscle appears to be at greater risk of injury than the outer subepicardial muscle for two major reasons:[21]

(1.) It receives less systolic blood flow than outer areas of the ventricle. Due to mechanical factors the muscle closest to the subendocardium thickens and contracts more vigorously during systole. The increase in systolic subendocardial pressure may literally collapse the subendocardial arteries; and

(2.) Subendocardial fibers contract more, probably developing greater tension, and therefore need more energy than fibers in other areas of the ventricle.

Experimental studies using oxygen electrodes have demonstrated about 30% less oxygen in the inner than outer layers of the ventricle.[22] Similarly, microspheres perfusing the coronary arteries of dogs have demonstrated about 10-20% more flow to the subendocardial muscle than the outer layer of the ventricle.[23,24] Thus, somewhat paradoxically, the subendocardial muscle is more hypoxic but yet receives greater coronary blood flow than the outer myocardial layers. Adequate subendocardial flow depends upon an adequate perfusion pressure and an adequate period of diastole. Diastolic hypotension, an increase in ventricular volume and pressure and tachycardia may lead to decreased subendocardial perfusion. It has been demonstrated in dogs by the use of diffusable radioactive indicators that partial coronary artery occlusion is accompanied by a disproportionately greater fall in subendocardial than subepicardial blood flow.[23] Similarly following coronary occlusion, myocardial infarction is more extensive in the inner than outer layers of the left ventricle. ATP levels also fall more quickly in the subendocardium than outer layers indicating that the subendocardium is more vulnerable to injury. If propranolol leads to an increase in end-diastolic volume and pressure and a reduction in systolic arterial pressure, it could theoretically lead to a reduction in blood flow to the inner muscle layers. If, on the other hand, catecholamines lead to a reduction in endocardial flow, by provoking tachycardia and by increasing oxygen needs and intramyocardial tension, this may be blocked by propranolol and improved subendocardial blood flow results. Microsphere studies in dogs indicate that propranolol does increase the ratio of blood flow to the subendocardium.[22] At present the evidence that similar changes occur in man with ischemic heart disease is not clear and the major effects of propranolol are still most likely those that effect heart rate, blood pressure, and contractility.

Dose-Response Relationships

It is apparent that the dose of propranolol given orally must be individually tailored to each patient.[25] In spite of nearly complete absorption from the gut, there is great variation in the serum levels of propranolol for a given dose between patients.[26] In subjects receiving 80 mg of propra-

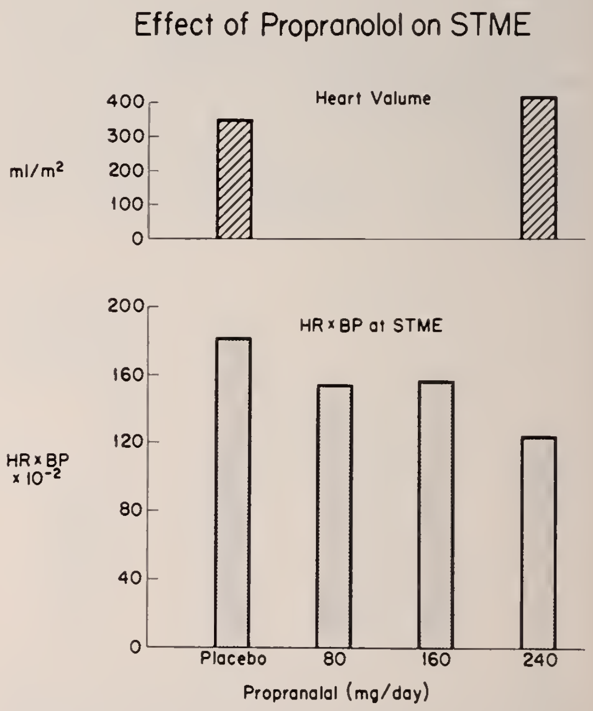

Fig. 4—During propranolol, there was a decrease in the HR X BP product at symptom tolerated maximum exercise (STME) and an increase in heart volume in the patient illustrated.

nolol orally daily the mean serum level is approximately 20 ng/ml, while with 160 mg/day the level is approximately 60 ng/ml. However, as much as a ten-fold difference in serum levels can be seen in different patients from an individual dose.[15,26] This very large variation has been attributed, by Shand, to individual differences in the ability of the liver to extract propranolol from the blood.[26] In fact, the hepatic extraction of propranolol is very great, and much of the drug is eliminated by the liver during its transfer in portal venous blood from the gut to the systemic circulation.[25-27] During chronic oral administration this extraction process becomes saturated so that the blood concentrations of propranolol accumulates.[27] In addition, propranolol may decrease cardiac output and secondarily reduce hepatic blood flow so that hepatic elimination is still further decreased.

When individual patients are compared, a direct relationship between blood level and improvement in exercise tolerance is not apparent.[15] In most instances a peak performance is reached at a blood level of 10-30 ng/ml with dissociation between performance and serum level at the high and low serum levels. In general a dose sufficient to reduce the exercising heart rate at the same level of exercise by 20% should bring good clinical relief of angina pectoris.

The lack of correlation between serum level and relief of angina pectoris may be related in part to "sympathetic tone". The intensity and frequency of sympathetic discharge, the catecholamine relief of angina in the heart, and the responsiveness of the receptors may vary greatly from patient to patient. It is not surprising, therefore, that no clear cut association between serum level and concentration can be found. Patients who develop angina pectoris at a high HR X BP product are more likely to benefit from propranolol therapy than those who become symptomatic at a low HR X BP product.

Propranolol has a relatively short half-life of the order of three to six hours following an oral dose for most people. It is customary, therefore, to prescribe propranolol four times daily. Larger doses given less frequently may be employed and have been found to be adequate in the treatment of hypertension.[28] Propranolol does have active metabolites and at least one (4-hydroxypropranolol), not measured by the standard propranolol assay, is known to contribute to Beta blockade after oral but not intravenous administration. Differences in plasma binding may also influence therapeutic effectiveness which is usually a function of the free drug present. Generally recommended procedures suggest commencing therapy with a small dose of propranolol e.g., 10 mg four times daily and increasing at three to seven day intervals to 160 to 320 mg/day. The dose may be increased until one achieves a reduction in the exercising heart rate of 20% or more or until side effects develop. Therapeutic failures should be considered when there is no clinical improvement with a dose of at least 320 mg/day, or when available, a serum level of 100 ng/ml is reached.

Side Effects

In an individual with bronchial asthma, propranolol may precipitate an acute attack.[29-31] In patients with chronic obstructive lung disease, however, where airway resistance is already very great, the 20% increase in airway resistance during propranolol therapy usually does not lead to a decrease in exercise tolerance[32] (Figure 5). Thus, in patients with both angina pectoris and chronic obstructive lung disease propranolol may be given cautiously with the expectation that exercise tolerance may be improved.

The more common unwanted effects of oral propranolol therapy are listed below and can be

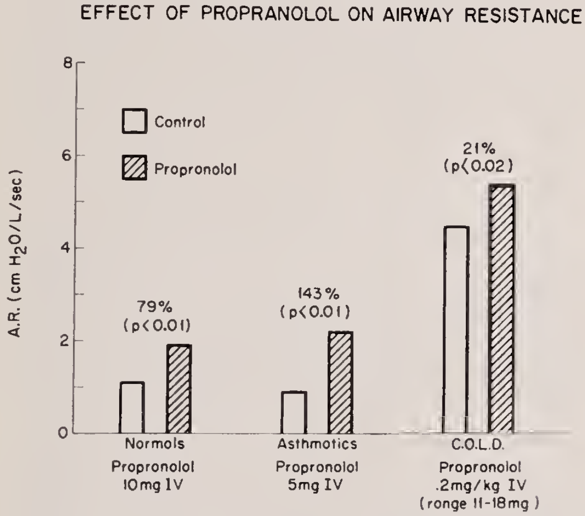

Fig. 5—The effect of propranolol on airway resistance. This figure represents a compilation of data adapted from several authors.[29-32] Although propranolol resulted in an increase in airway resistance in each of these groups of patients it was proportionately less in patients with chronic obstructive lung disease (C.O.L.D.).

divided into those secondary to the pharmacologic effects and those due to side effects.[33]

Pharmacologic Effects	% of Patients[33]
1. Cardiac failure	0.8%
2. Bradycardia and heart block	0.2%
3. Asthmatic attacks	0.5%
4. Hypotension	0.5%
5. Hypoglycemia	—

Side Effects	% of Patients[33]
1. Light-headedness	1.4%
2. Fatigue and Drowsiness	1.2%
3. Nausea and vomiting	1.0%
4. Diarrhea	0.5%
5. Sleeplessness	0.5%

Precipitation of left ventricular failure, bradycardia, and hypotension occur with nearly equal frequency. The most common side effects are fatigue, lethargy and light-headedness. Light-headedness may be secondary to a decrease in blood pressure in some patients. On the other hand, there is considerable evidence that propranolol has an effect on the central nervous system which is primarily depressive in nature and may be responsible for some of the drug's adverse effects. Impotence is not commonly associated with propranolol therapy. Strong contraindications to the use of propranolol are listed:

(1.) Bronchial asthma,
(2.) Sinus bradycardia (less than 45 bts/min),
(3.) Heart block,
(4.) Congestive heart failure,
(5.) Pulmonary hypertension with right ventricular failure, and
(6.) Adrenergic augmenting psychotropic drugs.

Symptoms with Sudden Withdrawal

The sudden withdrawal of propranolol from patients with stable angina pectoris may result in an increase in symptoms of ischemic heart disease to a level greater than present before propranolol therapy.[34-37] These symptoms have included not only an increase in frequency and severity of pain, but also the development of unstable angina, pain at rest, and in some instances myocardial infarction and sudden death. This withdrawal phenomenon is *not* frequent as indicated by several studies where patients in whom propranolol was suddenly withdrawn in preparation for surgery or coronary arteriography appeared to be at no greater risk than those patients who had not received propranolol.[38] The mechanism is not clear but studies of platelet aggregation suggest that an increase in platelet clumping follows propranolol withdrawal.[39,40] For this reason, it is suggested that propranolol withdrawal be tapered over a two-week period whenever possible.

Combination Therapy

One cannot leave the subject of the treatment of angina pectoris without including mention of nitrate therapy. It is noteworthy that the hemodynamic effects of nitrates and propranolol are such that each counteracts the oxygen wasting effects of the other. More and more evidence is accumulating that the effect of certain sublingual and chewable and perhaps oral nitrate preparations have an effect which may last for hours.[41-44] Nitrates reduce myocardial oxygen consumption by causing peripheral venous pooling, and a reduction in blood pressure thereby reducing both preload and impedance to blood flow, a reflex tachycardia may follow. These effects are helpful in reducing the increase in preload caused by propranolol which in turn may reduce the reflex tachycardia of nitrate therapy. Also noteworthy is the fact that in experimental animals, nitroglycerin, as well as propranolol, increases subendocardial blood flow. Although a number of such studies are available, data published by Dagenais, et al., (Figure 6), indicates that while propranolol allowed an increase in external work of 53%, the combination of propranolol with a nitrate allowed a striking increase in external work (100%) with little change in the heart rate at the onset of chest

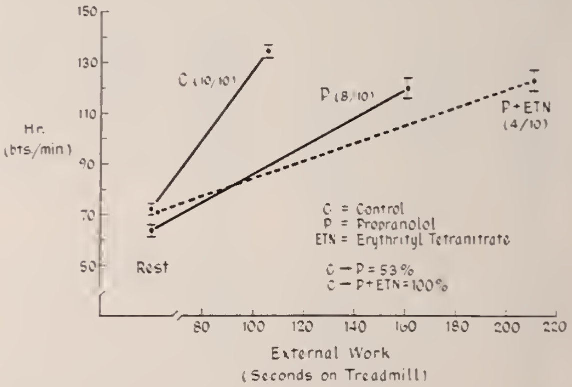

Fig. 6—Symptom tolerated maximum exercise in angina pectoris (data adapted from Dagenais et al.).[42] The combination of propranolol and nitrate therapy allows more external work to be performed than with propranolol alone.

pain.[42]

Conclusions

Propranolol is effective therapy in angina pectoris. Its efficacy is derived mainly from its ability to reduce heart rate, blood pressure and contractility, major determinants of myocardial oxygen consumption. Further data is needed to assess its effect on subendocardial blood flow. Since the exact role of coronary artery surgery in patients with angina pectoris is controversial at present, we prefer to limit surgery to those patients who do not experience sufficient relief of pain during medical therapy. Our therapeutic regimen consists first of modifying risk factors such as smoking and high blood pressure. Sublingual nitroglycerin is given for the relief of chest pain and for prophylactic use for activities which predictably cause chest pain. Isosorbide dinitrate, sublingually, is added to the therapeutic regimen in a dose to the patient's tolerance or sufficient to alleviate symptoms. In those patients who remain symptomatic, propranolol is added at this point in the therapeutic program.

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Prenatal Assessment of Intrauterine Growth Retardation

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Approximately 8% of infants born in the United States have low birth weight (2,500 g or less), and these infants account for 75% of all neonatal deaths. About one-third of these low-birth-weight infants have retarded intrauterine growth. Surviving neonates are at an increased risk for cerebral palsy and other adverse neurologic sequelae. Important in this problem are the specific fetal, maternal, and environmental factors associated with intrauterine growth retardation, as well as the clinical, biochemical, and biophysical techniques used to evaluate fetal growth and well-being before birth.

THE OBSTETRICIAN WHO assumes responsibility for maternal safety and fetal well-being must be cognizant of all the factors that may alter an ideal outcome of pregnancy. This paper surveys the problem of the small-for-date fetus, its recognition, and its clinical management.

Neonatal Risk Factors

About 8% of infants born in the United States are of low birth weight (2,500 g or less), and 75% of all neonatal deaths are derived from this group.[1,2] These low-birth-weight infants have a 30-fold increased risk of death during the neonatal period. About one-third of the low-birth-weight infants have had intrauterine growth retardation and are best classified as being small for gestational age.[2] The total problem is best understood by realizing that, in addition to mortality risks, these growth-retarded neonates are at increased risk for such clinical sequelae as cerebral palsy, epilepsy, mental retardation, and minimal cerebral dysfunction.[3,4] Prospective and retrospective studies have shown that the factors associated with perinatal mortality also are associated with these neurologic morbidities in the surviving infants.[4]

The classification of the newborn by both birth weight and gestational age, as suggested by Battaglia and Lubchenco in 1967,[5] made it possible to categorize the newborn into risk groups that may be meaningfully related to morbidity and mortality statistics. Thus, the high-risk fetus can be quickly identified and appropriately treated.

In the past, many studies of newborns have used either birth weight or length of gestation to divide the "premature" from the "mature" group.[6] In 1950, the World Health Organization[7] arbitrarily selected 2,500 g as the lower limit of maturity. This division was selected because infants weighing less than 2,500 g are less likely to survive and, as birth weight decreases, mortality tends to increase. Likewise, if gestational age of 37 weeks is chosen as the dividing line between "premature" and "mature" infants, the shorter the gestational age, the greater are the chances of neonatal death or significant neurologic deficits.[8] However, closer investigation shows that infants who have birth weights of less than 2,500 g do not reflect a uniform gestational age. In a review of 400,000 single live births, Yerushalmy[6] reported that 45% of the infants less than 2,500 g at birth had a gestational age of 37 weeks or more. These infants had retarded rates of intrauterine growth, as contrasted with those infants who had both short gestational age and low birth weight.

Battaglia and Lubchenco[5] related neonatal mortality to birth weight *and* gestational age (Figure 1). Notable is the much improved survival rate of the 1,500-g, small-for-gestational-age infant, as compared with the 1,500-g preterm infant. It is known that for any constant birth weight the

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See editorial, page 623.

mortality rate decreases as gestational age increases and for any given gestational age the mortality rate decreases as birth weight increases up to about 4,000 g.

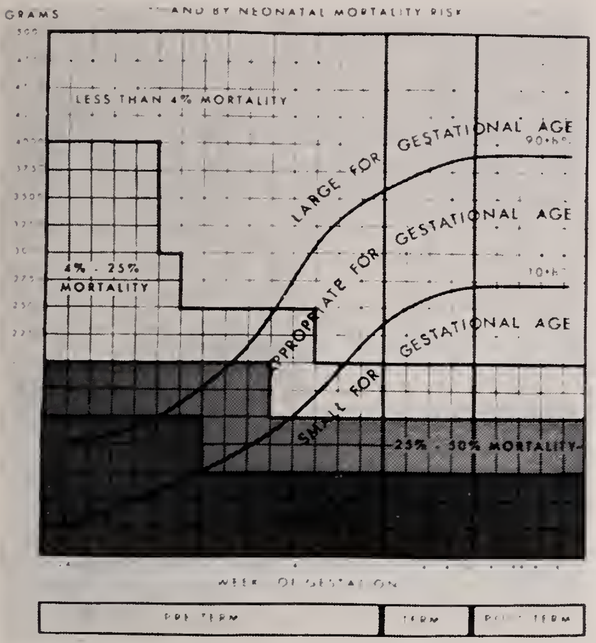

Fig. 1—University of Colorado Medical Center classification of newborns by birth weight and gestational age and by neonatal mortality risk. (From Battaglia, F. C. and Lubchenco, L. O., A practical classification of newborn infants by weight and gestational age. J. Pediatr. 71:159, 1967. By permission of the C. V. Mosby Company.)

Behrman and Babson[9] used the system of Battaglia and Lubchenco[5] to construct a similar graph, based on 40,000 births in Portland, Oregon. They stressed that use of this graph immediately classified the newborn into low-, medium-, and high-risk groups and allowed the infant to be given appropriate intensive care.

The small-for-gestational-age infant may be preterm (less than 38 completed weeks in utero), term (38 to 42 weeks), and post-term (42 weeks or more). The causes of retarded intrauterine growth rate may be divided into factors that primarily affect the fetus and its intrinsic growth potential and maternal or placental conditions that compromise the fetal nutrition[10e,11,12f,13] (Table 1).

Data on infants with certain fetal anomalies and infants from various complicated pregnancies show that there are definite "clusters" for each specific condition about a median birth weight and gestational age[14] (Figure 2). These data contribute to the study of specific disease processes and provide the neonatalogist with another tool for the assessment of the newborn.

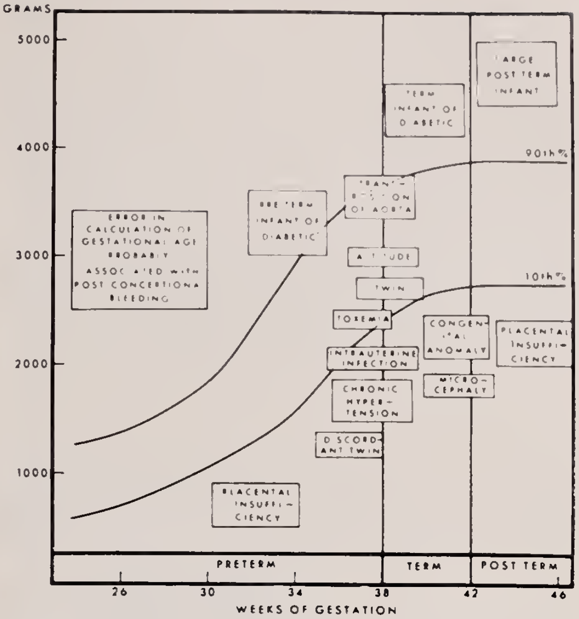

Fig. 2—Conditions associated with deviations of intrauterine growth that may be assoicated with significant morbidity, represented graphically to indicate the approximate birth weight and gestational age at which the condition is likely to occur. (From Nutricia Symposium: Aspects of Praematurity and Dysmaturity, Groningen, Holland, 1967. Jonxis, J. H. P., Visser, H. K. A. and Troelstra, J. A. (eds.). Stenfert Kroese, Leiden, Holland, 1968. By permission.)

Conditions Associated with Intrauterine Growth Retardation

Fetal Factors: Genetic Disorders

The exact pathophysiology of growth arrest seen with Down's syndrome, Turner's syndrome, and other chromosomal abnormalities and heritable disorders of development is primarily speculative.[15] The chromosome imbalance in these abnormal gestations produces a continuum of growth failure that includes retarded intrauterine growth, spontaneous abortion, stillbirth, neonatal death, postnatal growth retardation, and diminished life-span for the survivors.[15]

Maternal Factors: Systemic Disease

If intrinsic genetic defects of the embryo are not present, inadequate intrauterine nutrition must be the cause of intrauterine growth failure. This generalization may be applied to the maternal factors of systemic disease, intrauterine infection, environmental and situational conditions, as well as placental and uterine disease (Table 1).

The hypertensive disorders of pregnancy, including preeclampsia-eclampsia and chronic maternal hypertension antecedent to pregnancy, are well-recognized as being associated with maternal death, stillbirth, and neonatal death.[12c] Ounsted and Ounsted[16] emphasized that opinions vary on the precise relationship of these hypertensive disorders to intrauterine growth retardation. However, most large demographic studies, such as the British Perinatal Mortality Survey, have shown a positive association between severe hypertensive disease and low birth weight.[16] In these hypertensive disorders, fetal growth retardation is considered to be caused by compromised maternal blood supply to the placenta, with resulting fetal malnutrition.[3]

Generally, the infant of the diabetic mother is large for his gestational age. This increased size (fetal macrosomia) affects all organs of the fetus, except the brain, and is due, in part, to excessive

TABLE 1

Some Conditions Associated With or Causing Intrauterine Growth Retardation

I. Fetal factors
    A. Chromosomal aberrations and heritable disorders of development
        1. Down's syndrome
        2. Turner's syndrome
        3. Seckel's syndrome (bird-headed dwarfism)
        4. Silver's syndrome
        5. Cornelia de Lange syndrome
        6. Osteogenesis imperfecta
        7. Anencephaly
II. Maternal factors
    A. Systemic disease
        1. Preeclampsia-eclampsia
        2. Hypertensive cardiovascular disease
        3. Diabetes (severe)
        4. Ulcerative colitis
        5. Hyperthyroidism or hypothyroidism
        6. Malignancy
        7. Anemias
        8. Pyelonephritis
    B. Intrauterine infection
        1. Rubella (German measles)
        2. Cytomegalic inclusion disease
        3. Herpesvirus hominis
        4. Coxsackievirus B
        5. Hepatitis virus A
        6. Toxoplasmosis
        7. Syphilis
        8. Tuberculosis
        9. Listeriosis
        10. Malaria
    C. Environmental and situational (potentially correctable) conditions
        1. Malnutrition
        2. Limited weight gain or weight loss in third trimester
        3. Multiparity—infant born after four pregnancies
        4. Close spacing of pregnancies
        5. Cigarette smoking
        6. Drug addiction
        7. Hypoxia related to high altitude, maternal cardiac disease, or hemoglobinopathy
        8. Previous poor obstetric performance
    D. Placental and uterine disease
        1. Aging placenta in postmaturity
        2. Bicornuate uterus
        3. Abnormal cord insertions (velamentous, battledore, two-vessel cord)
        4. Circumvallate placenta
        5. Diffuse fibrinosis and placental infarctions (rare)
        6. Placental hemangiomas (rare)
        7. Parabiotic transfusion in a monochorionic twin placenta (rare)

fat deposition.[12d,17] Unexplained intrauterine death after the 36th week of gestation, dystocia from fetal macrosomia, and an increased incidence of respiratory distress syndrome in the newborn period are problems common to the diabetic gestation.[18] One possible mechanism for the excess fetal fat deposition is the fetal hyperinsulinism and hypertrophy of the pancreatic islet-cells that result from chronic maternal and fetal hyperglycemia. The association of meticulous control of maternal glucose levels in diabetic gestations with a lowered incidence of excessive birth weights is clinical evidence that hyperinsulinism may be the cause of fetal macrosomia.[17]

In more severe maternal diabetes with pelvic vascular disease, the fetal macrosomia may be modified by placental insufficiency and intrauterine growth retardation, with the resultant production of a small-for-gestational-age newborn.[17] Because fertility is less common in these severely diabetic women, fewer growth-retarded diabetic gestations are seen. When the obstetrician has an opportunity to counsel a young diabetic woman who desires pregnancy, he should educate her in regard to the special significance of knowing her exact menstrual dates, avoiding excessive weight gain, and following strict dietary and medical management of her diabetes during pregnancy.

Maternal anemia is related to low-birth-weight infants as well as to increased perinatal morbidity and mortality.[19] Macgregor,[20] in Kenya, showed that 42% of women who had hemoglobin levels of less than 7.5 g/dl delivered low-birth-weight infants, as compared with an incidence of 12.7% for mothers who had hemoglobin levels more than 9.0 g/dl. Whether the disturbed fetal growth in anemia is caused by secondary intrauterine hypoxia or by maternal malnutrition that often accompanies the anemia is not clear. Both factors probably are important in altered fetal development.

Intrauterine Infection

Such infection is acquired by transplacental passage of viruses, bacteria, and certain protozoa and is an important cause of retarded intrauterine growth, as well as of anomalous fetal development, fetal death in utero, premature labor, stillbirth, and spontaneous abortion. In 1941, Gregg[21] first reported maternal rubella (German measles) in early pregnancy as a cause of severe congenital malformations in the newborn. Analysis of data acquired in the rubella pandemic of 1963 and 1964 has made this the classic example of congenital viral intrauterine infection.[22] A study of 58,828 pregnancies in the Collaborative Perinatal Research Study revealed that approximately 5% of gestations were complicated by viral infection, exclusive of the "common cold."[23] Influenza, flu-like illness, herpes-virus infections, and viral gastroenteritis were the common offenders. Of the dozen or so viruses known to reach the human fetus, only rubella, cytomegalovirus, and herpes virus hominis are known to be teratogenic.[23] Coxsackie virus B, hepatitis virus A, influenza virus, and mumps virus are questionably related to various fetal maldevelopments.[10a] Other nonviral diseases important in fetal wastage include toxoplasmosis, caused by the protozoan intracellular parasite *Toxoplasma gondii,* syphilis tuberculosis, listeriosis, and malaria.[12e,23]

Infection with rubella, cytomegalovirus, herpesvirus hominis, toxoplasmosis, and syphilis may produce similar clinical findings. The neonates congenitally infected with any one of these agents may have the following features in common:[10f,22] (1) small for gestational age; (2) low birth weight; (3) hepatosplenomegaly; (4) early jaundice with increased "direct" bilirubin; (5) petechiae, purpura, or vesicular rash; (6) chorioretinitis, keratitis, conjunctivitis, cataracts, and microphthalmia; (7) congenital anomalies; and (8) anemia with evidence of hemolysis. The degree to which the fetus is affected is related to the period of gestation during which the infectious agent was introduced. In general, the earlier in the gestation the infestation occurs, the more severe are the results in the fetus or newborn.[22]

Environmental Conditions

Certain details of the mother's environment, habits, and past obstetrical history, listed in Table 1, are related to intrauterine growth retardation, and thus these help to further identify the pregnancy at risk. The effect of severe maternal malnutrition on birth weight was demonstrated by Dutch women during the famine of World War II. Smith[24] reported that the median in birth weight was down 240 g, or a reduction of about 7%, for infants born in Rotterdam during the starvation of 1944. His studies also showed that maternal starvation does not significantly limit fetal birth weight until the third trimester of pregnancy.

Many low-birth-weight infants today come from the less-developed countries of the world where poor maternal diet is considered to be one of the main contributing factors.[25] Socioeconomic conditions generally link maternal malnutrition to other factors known to be prejudicial to optimal fetal development, such as poverty, chronic maternal disease, poor hygiene, closely spaced pregnancies, and multiparity.[26] These coexistent variables make it difficult to quantitate the effect of maternal malnutrition on intrauterine growth.

Cigarette smoking during pregnancy is related to an increased incidence of spontaneous abortion and a reduced rate of fetal growth.[16,27] Data from the British Perinatal Mortality Survey show that low birth weight was seen almost twice as often in the infants of women who smoked during pregnancy.[16] Herriott and co-workers[28] showed that, even when mothers stopped smoking early in pregnancy, they still produced smaller babies than did nonsmoking mothers. Several studies[29,30] also have noted the peculiar finding that smoking is associated with less preeclamptic toxemia, in addition to low birth weight. If the deleterious effects of smoking are explained to the young pregnant woman, she will often be sufficiently motivated to decrease or discontinue her smoking.

Intrauterine growth is sensitive to high altitude, and mothers living at high altitudes have given birth to infants of lower mean birth weight than did mothers of infants born at lower altitudes.[16] The intrauterine growth curves of Lubchenco and associates[31] were based on deliveries in Denver, Colorado, which is more than 5,000 feet above sea level. If these curves are compared with the curves of Babson et al.[32] obtained in Portland, Oregon, which is near sea level, the Denver curves show a lower birth weight for all stages of gestation.

Recognizing that poverty, maternal malnutrition, environment, chronic maternal disease, and other factors that adversely affect the mother and fetus do not usually change or improve from one pregnancy to the next, it is not surprising that poor reproductive performance tends to be repetitive. Poor obstetric history is a marker of the high-risk gestation in itself because patients tend to develop the same problems from one gestation to the next.[1,25] In 1960, a perinatal mortality study[33] involving 25,984 pregnancies in Ontario, Canada, showed that mothers with a previous low-birth-weight delivery were at more than a threefold increased risk for a subsequent low-birth-weight infant. Data on 60,000 pregnancies were gathered in the collaborative perinatal study[34] of the National Institute of Neurological Diseases and Stroke to determine the relationship between past obstetric performance and future reproductive outcome. In that study, mothers whose last pregnancy resulted in a low-birth-weight infant had a 50% increased risk for fetal death in the subsequent pregnancy and a fourfold increased risk for another low-birth-weight infant. Yerushalmy[6] showed that a woman who, in her previous pregnancy, produced a preterm (less than 37 weeks) and low-birth-weight infant (2,500 g or less) is expected to produce another preterm, low-birth-weight infant rather than a term, low-birth-weight infant or a preterm, appropriate-birth-weight infant, or some other combination. Thus, the specific combination of birth weight and gestational age that was produced in a previous pregnancy is likely to be repeated.

Multiple pregnancy results in both prematurity and intrauterine growth retardation.[35] McKeown and Record[36] studied growth rates of twins, triplets, and quadruplets and found that intrauterine growth was progressively limited as litter size increased (Figure 3). Their study showed that linear growth begins to decrease at about 36 weeks for singleton pregnancies, 30 weeks for twin pregnancies, 27 weeks for triplet pregnancies and 26 weeks for quadruplet pregnancies.

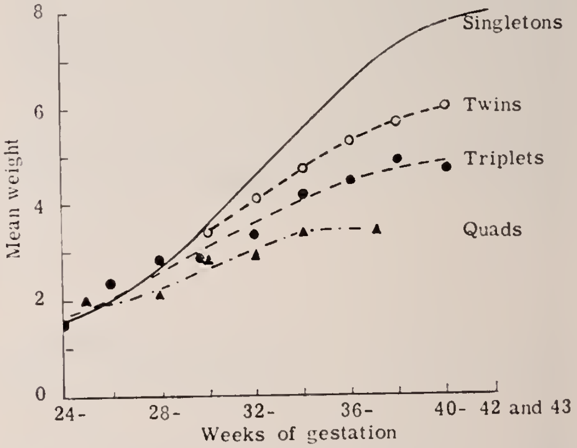

Fig. 3—Mean birth weight of single and multiple fetuses related to duration of gestation (cubic curves fitted by the method of least squares). (From McKeown, T. and Record, R. G. Observations on fetal growth in multiple pregnancy in man. J. Endocrinol. 8:386, 1952. By permission.)

Placental and Uterine Disease

Placental vascular anastomoses (intrauterine parabioses) are seen most often with monovular, monochorionic twins and may result in notable disparity in the size of the twins at birth[12b,37] (Figure 4). If the twin-to-twin transfusion is excessive, the smaller twin may die in utero and be retained until the end of pregnancy. This blighted twin is known as a fetus papyraceous (Figure 5). Just as multiple gestation limits intrauterine development to some extent, other conditions such as postmaturity, bicornuate uterus, abnormal cord insertions, placental infarcts, and placental hemangiomas may limit fetal nutrition and growth.[13]

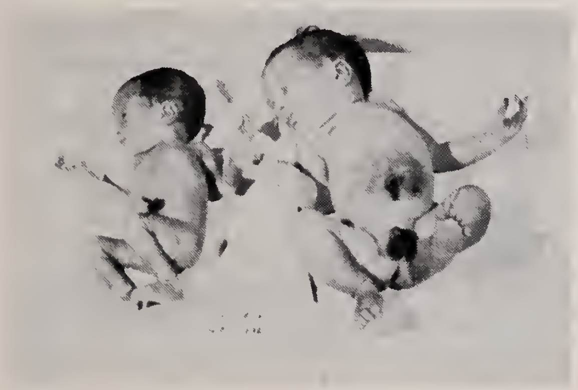

Fig. 4—Twin infants born to 32-year-old white woman, gravida III, para 2, with preeclampsia at 36 weeks' gestation. Birth weights were 1,135 and 2,750 g, head circumferences 22 and 33.5 cm, lengths 40 and 49.5 cm, with marked plethora and dysmaturity in smaller twin. (From Andrews, B. F., Lorchirchoonkul, U. and Shott, R. J. Small-for-date babies. Pediatr. Clin North Am. 17:185, February 1970. By permission of the W. B. Saunders Company.)

Techniques for Assessing Fetal Growth

Clinical Observations

Basic clinical observations are used by obstetricians to assess fetal growth and intrauterine development and to estimate the duration of pregnancy. An attempt is made to obtain an accurate date of the first day of the last menstrual period so that Naegele's rule may be used to calculate the expected date of delivery. Bimanual examinations correlate the uterine size with the calculated gestational age. Measurements of progressive maternal weight gains and progressive increase in fundal height are recorded at each prenatal visit. The dates of "quickening" (18 to 20 weeks), "lightening" or engagement of the fetal head (about 38 weeks), and the first auscultation of fetal heart tones with the head stethoscope (about 20 weeks) are all carefully noted.[10b,12a,38]

Biochemical and Biophysical Methods

These methods can evaluate more precisely the pregnancy during gestation and in the critical labor and delivery period (Table 2). The multiplicity of tests and diagnostic techniques reflects a well-accepted fact: that no single test is completely adequate for predicting fetal well-being before delivery.[39a,23,55,56]

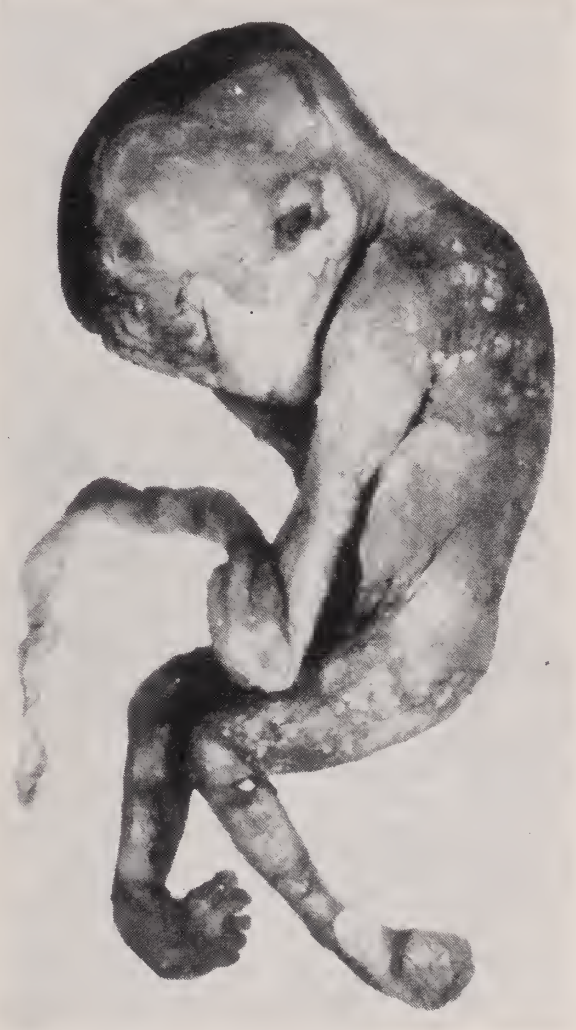

Fig. 5—Fetus papyraceous. Probably the result of a germinal defect; growth arrested in 20th week. Twin pregnancy at term; other infant was normal. (Carnegie Collection No. 4159A.) (From Hellman, L. M., Pritchard, J. and Wynn, R. M.: Williams Obstetrics, 14th edition, Appleton-Century-Crofts, New York, 1971, p. 666. By permission of Carnegie Institution of Washington, Department of Embryology, Davis Division.)

TABLE 2

Some Biochemical and Biophysical Techniques for Assessment of Fetus During Gestation and Labor*

I. Fetal maturity
- A. X-ray techniques that measure appearance of specific epiphyseal ossification centers[39b]
  - 1. Distal femoral epiphysis (36 weeks)
  - 2. Proximal femoral epiphysis (38 weeks)
- B. Ultrasound techniques
  - 1. Fetal cephalometry—a biparietal diameter >8.7 cm correlates well with fetal weight >2,500 g
  - 2. Hourly fetal urine-production rate-bladder contents may be ultrasonically measured and correlated with fetal menstrual age from 30 to 40 weeks[40]
- C. Amniotic fluid studies
  - 1. Lecithin-sphingomyelin (L/S) ratio—if ≥2.0, pulmonary maturity is sufficient for extrauterine survival
  - 2. Lecithin concentration—if ≥3.5 mg/dl, respiratory distress syndrome is unlikely
  - 3. Fetal fat cells—if ≥20%, delivered infants are not premature[41]
  - 4. Creatinine—if ≥2 mg/dl, the gestation is 36 weeks' duration or more[42]
  - 5. Bilirubin—unconjugated bilirubin detected by its spectrophotometric peak at $450 m\mu$ wavelength decreases to 0.00 optical density at 36 weeks' gestation[43]
  - 6. Enzymes heat-stable alkaline phosphatase, diamine oxidase, oxytocinase, and lactic dehydrogenase are related to gestational age
  - 7. Osmolality decreases as pregnancy advances; fetal maturity is suggested by solute concentration of 250 mosmol/liter/kg or less
  - 8. α-fetoprotein levels decrease with advancing gestation and are less than 185 mg/ml at 37 weeks[44]
  - 9. Hydroxyproline—low concentrations are associated with small-for-date babies[45]
  - 10. Transferrin—concentration may increase with gestational age[46]
  - 11. Insulin—concentration increases with gestational age[47]
  - 12. Adenosine-3′,5′-monophosphate (cyclic-AMP) may be derived from fetal kidney; its concentration increases with advancing gestation[48]

II. Fetal growth
- A. Ultrasound
  - 1. Serial fetal cephalometry with measurements of growth rate of fetal biparietal diameter demonstrates intrauterine growth retardation from 20 weeks gestation to term[39c]
  - 2. Reduced hourly fetal urine-production rate reflects intrauterine fetal growth retardation[40]
- B. Amniotic fluid
  - 1. Albumin fraction and total proteins decrease as pregnancy progresses, but this is a poor indicator of gestational age[43,49]
  - 2. Serine-proline and serine-phenylalanine ratios increase with advancing gestation
  - 3. Insulin levels increase as fetus enlarges
- C. Maternal leukocyte changes in morphology are linked to fetal growth
- D. Maternal estrogen excretion—24-hour estriol excretion increases with fetal size, and patients with intrauterine growth retardation have low values
- E. Maternal serum transferrin correlates with infant birth weight

III. Fetal well-being before labor
- A. Master "2-step" exercise test may cause fetal bradycardia or tachycardia in high-risk pregnancy
- B. Oxytocin challenge test—if "positive," it produces late decelerations of fetal heart in compromised fetus
- C. Amnioscopy to study amniotic fluid
  - 1. Meconium staining indicates fetal hypoxia
  - 2. Decreasing amniotic fluid volume is seen with prolonged pregnancy or failing placental function
  - 3. Fetal bleeding may be checked if amniocentesis has resulted in a "bloody tap"
- D. Amniocentesis
  - 1. Amniotic fluid erythropoietin levels are higher with anemic and hypoxic fetuses
  - 2. Amniotic fluid lactic dehydrogenase levels are elevated with fetal hypoxia
  - 3. Dye injected into amniotic fluid is swallowed more rapidly by fetuses of toxemic mothers
- E. α-fetoprotein levels in maternal plasma are elevated with placental insufficiency, with spina bifida and anencephaly, severe Rh immunization, esophageal atresia, nephrosis, and fetal death
- F. Pre-ejection period of fetal cardiac cycle varies with hypoxemia and may be monitored before and during labor[50]

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*Data from Kelly, J. V., Diagnostic techniques in prepartal fetal evaluation. Clin Obstet Gynecol 17:53, September 1974, except where specifically referenced.

TABLE 2 (continued)

- IV. Placental function tests
  - A. Serial 24-hour maternal urinary estriol levels normally increase with advancing gestation
  - B. Maternal plasma clearance of dehydroepiandrosterone sulfate is reduced in patients with preeclampsia and severe hypertension
  - C. Maternal serum oxytocinase (cystoaminopeptidase) is reduced in fetal death, toxemia, and dysmaturity[10d]
  - D. Human placental lactogen in maternal serum is lowered in hypertension, postmaturity, and threatened abortion
- V. Miscellaneous
  - A. Angiotensin-sensitivity test is a promising screening test that selects the patient destined to develop preeclampsia early during third trimester before any clinical signs are present[51]
  - B. Maternal synalbumin antagonism is increased in diabetic mothers who give birth to large infants
  - C. Urinary ratios of potassium to creatinine and sodium to creatinine are lower than normal at 36 weeks in patients who later develop preeclampsia
- VI. Fetal well-being during labor
  - A. Direct fetal monitoring of fetal electrocardiogram by scalp electrode application and uterine activity by transcervical intrauterine catheter[52]
    - 1. Early deceleration (type I dip) indicates head compression and is usually not serious
    - 2. Late deceleration (type II dip) reflects placental insufficiency and fetal asphyxia
    - 3. Variable deceleration is related to umbilical cord compression and is usually innocuous
    - 4. Loss of the normal baseline beat-to-beat variability of 3 to 5 cycles/s is seen in compromised fetus
  - B. Measurement of intrapartum acid-base status by fetal scalp blood sampling[53b]
    - 1. Fetal pH <7.25 should be rechecked
    - 2. Fetal pH of $\leqslant 7.20$ indicates fetal distress
  - C. Intrapartum electroencephalographic monitoring[54]

Estrogen

The measurement of estrogen excretion is probably the most commonly used biochemical index of pregnancy status by most centers in the world.[57] In 1928, Aschheim and Zondek[58] noted increasing titers of estrogens in the urine and blood of pregnant women as gestation progressed. Although more than 20 estrogens have been identified in the human, more than 90% of the total urinary estrogen content in the pregnant woman is estriol.[59] The biosynthesis of estriol by the placenta is dependent on a precursor substance produced by the fetal adrenal glands, 16α-hydroxydehydroepiandrosterone.[60] Because of this metabolic interrelationship, serial measurements of 24-hour urinary estriol excretion are regarded as a test of the fetoplacental unit.

Greene and associates[61] showed that 24-hour urinary estriol values of less than 2 mg at term are predictive of fetal death; values between 2 and 4 mg are suggestive of fetal distress; and values of more than 12 mg are indicative of a normal gestation. A wide range of values exists for 24-hour estriol excretion as the normal pregnancy approaches term (Figure 6).[62] Because of this variation in the normal range, serial measurements should be taken to determine the estriol excretion pattern for a specific gestation. Consistently low maternal estriol excretion is seen with intrauterine growth retardation.[63] Greene and Beorgie[64] stated that it is rarely practical to study estriol excretion before the 34th week of gestation because of the inability to salvage such a gestation even if de-

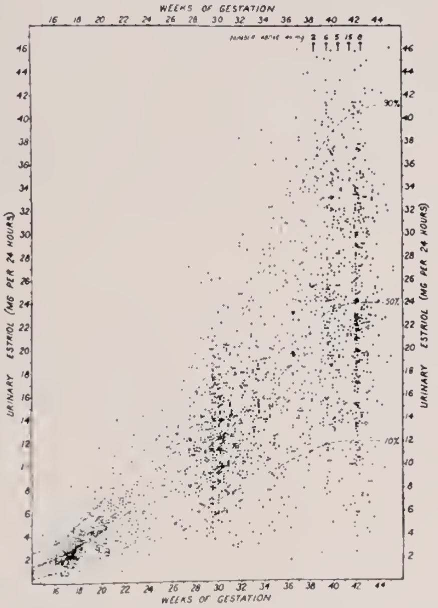

Fig. 6—Estriol values from 14 weeks of gestation, showing 10th, 50th, and 90th percentiles. (From Beischer, N. A., Brown, J. B., Smith, M. A. and Townsend, L., Studies in prolonged pregnancy. II. Clinical results and urinary estriol excretion in prolonged pregnancy. Am. J. Obstet. Gynecol. 103:483, 1969. By permission of the C. V. Mosby Company.)

creasing levels are noted. They recommended that estriol studies be done to detect intrauterine growth retardation, as well as to aid in the management of pregnancies complicated by hypertension, diabetes, preeclampsia, and other risk factors.

Ultrasound

Diagnostic ultrasound employs a directed beam of ultrasonic vibrations which are reflected at the interface between tissues with different acoustic impedances.[65a] The reflected beam, or echo, returns to the propagating source, where a piezoelectric crystal converts its energy to an electric impulse that may be displayed on an oscilloscope screen. The distance of the reflecting interface from the propagating source may be calculated by measuring the time it takes the echo to return.[39b] Ultrasonic echo measurement of the biparietal diameter is accomplished by directing the ultrasonic beam perpendicularly to the fetal head. Biparietal diameter growth curves throughout the second and third trimesters as determined by serial ultrasonic cephalometry are shown in Figure 7. The growth rate of the fetal head is nearly linear until it slows at about 30 weeks of gestation.[56] Many studies have correlated growth of the fetal biparietal diameter with intrauterine fetal growth, weight, and maturity.[66-68] Dewhurst and co-workers[69] showed that serial ultrasonic biparietal measurements identified the growth-retarded fetus more reliably than did a reduction in 24-hour estriol excretion. A recent study by Robinson et al.[70] demonstrated that the combination of sonar cephalometry and 24-hour urinary estriol assays is highly predictive of intrauterine growth retardation. There have been no reports of damage to the mother or fetus by diagnostic ultrasound.[65b] Ultrasound is an objective, noninvasive technique for the evaluation of intrauterine growth rate, identification of an early gestational sac, diagnosis of hydatidiform mole, placental localization, and study of gynecologic tumor masses.[10c]

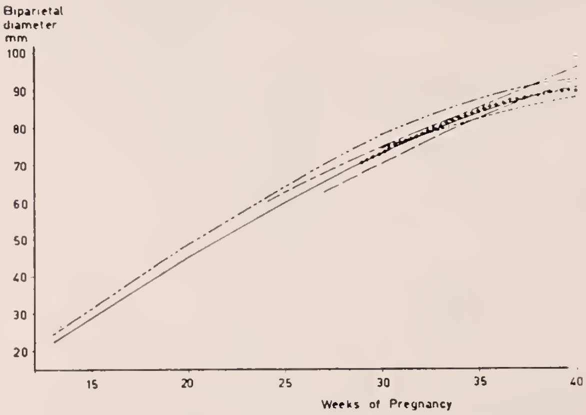

Fig. 7—Fetal biparietal diameter, mean values. (From Levi, S. and Smets, P., Intra-uterine fetal growth studied by ultrasonic biparietal measurements. Acta Obstet. Gynecol. Scand. 52:193, 1973. By permission.)

Phospholipids

Respiratory distress syndrome (hyaline membrane disease) is the commonest cause of death among preterm infants. In 1967, Brumley and coworkers[71] demonstrated that the lungs of infants who died from hyaline membrane disease had a low phospholipid content. Phospholipid material (surfactants) lines the alveoli and is necessary for adequate alveolar expansion and gaseous exchange at birth. Dipalmityl lecithin is the major phospholipid in the lung.[72] In 1971, Gluck and associates[73] studied 302 samples of amniotic fluid and showed that the ratio of lecithin to sphingomyelin (another surface-active phospholipid) could be used to predict pulmonary maturity. They demonstrated a sudden increase in lecithin concentration and a decrease in the sphingomyelin concentration at about 35 weeks of gestation, resulting in a lecithin-to-sphingomyelin (L/S) ratio of two or greater (Figure 8). Numerous clinical

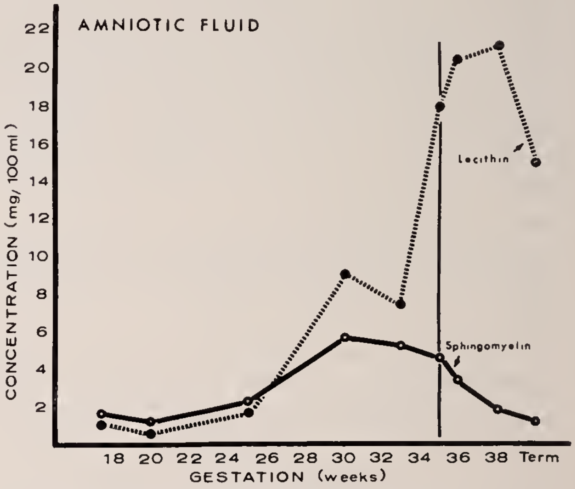

Fig. 8—Mean concentrations in amniotic fluid of sphingomyelin and lecithin during gestation. Acute increase in lecithin level at 35 weeks marks pulmonary maturity. (From Gluck, L., Kulovich, M. V., Borer, R. C., Jr., Brenner, P. H., Anderson, G. G. and Spellacy, W. N., Diagnosis of the respiratory distress syndrome by amniocentesis. Am. J. Obstet. Gynecol. 109:440, 1971. By permission of the C. V. Mosby Company.)

trials have supported these findings and, in general, an L/S ratio of 2.0 or greater is accurate in predicting pulmonary maturity in 85% of cases.[56] Conditions that predispose to intrauterine growth retardation, for example, toxemia, hypertension, maternal drug addiction, chronic retroplacental hemorrhage, and servere diabetes, are often associated with accelerated pulmonary maturity, while delayed maturation is seen with classes A, B, and C diabetes.[74]

Oxytocin Test

The oxytocin challenge test has been used to study pregnancies that are at risk because of placental insufficiency, such as those complicated by diabetes, hypertension, toxemia, postmaturity, and intrauterine growth retardation.[75] The test, also known as stressed cardiotocography, the Pit test, and the oxytocin function test, consists of the induction of regular uterine contractions by the intravenous administration of oxytocin and the monitoring of the fetal heart rate pattern during these contractions. The result is positive if contractions produce late decelerations of the fetal heart and is negative if there are no decelerations after 30 minutes of induced uterine activity.[53a] Ray and associates[75] studied 66 patients by the oxytocin challenge test. Patients with a negative test result were retested in one week. There were no intrauterine deaths or decreasing estriol values within one week of a negative result. However, there were three intrauterine deaths within 72 hours of a positive stress test. In most cases, a positive oxytocin challenge test was associated with a low 24-hour estriol excretion and the birth of a stillborn or depressed fetus, but some patients had normal estriol excretion levels at the time of the first positive challenge test and then had a subsequent decrease in estriol excretion two or three weeks after the first positive challenge test. In 40 of 43 patients with a negative challenge test, the Apgar score at birth was seven or higher. A negative result probably means that the fetus will survive at least another week in utero and is not in jeopardy.[53a]

Summary

The practitioner should be aware of the problem of intrauterine growth retardation and its relationship to poor pregnancy outcome. Use of all the well-established clinical observations of fetal development during prenatal visits aids identification of the growth-retarded fetus. These clinical observations may be augmented by measurements of estriol, ultrasonic cephalometry, determination of L/S ratios from amniotic fluid, and perhaps the oxytocin stress test to determine the optimal time for delivery. During labor, the use of fetal electrocardiographic monitoring and scalp vein blood sampling should further assist in the optimal delivery outcome of these high-risk gestations. When difficulties in the neonatal period are anticipated, every effort is made to accomplish delivery of a viable infant who may maximally benefit from modern pediatric care during the transition to an extrauterine environment.

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Southern Minnesota Medical Association

The annual meeting of the Southern Minnesota Medical Association will be held September 25, in Albert Lea. The Kahler Motel is the meeting place. Contact: Ethel A. McClane, Secretary, 1726 No. 4th St., Mankato 56001.

Program

9:00 A.M.	Fetal Phenytoin Syndrome—A Sibling Incrimination of Diphenylhydantoin as a New Teratogenic Agent.—Joseph S. Emond, Jr. M.D.
9:10 A.M.	Spontaneous Perforation of Diverticulum of Distal Esophagus.—Alan Stalheim, M.D.
9:20 A.M.	Crohn's Colitis—Recognition and Complications—Carl E. Christenson, M.D.: Stanley M. Goldberg, M.D.; Jerry L. Schottler, M.D.; E. G. Balcos, M.D.
9:40 A.M.	Steffee Arthroplasty of the Metacarpophalangeal Joints—Ronald L. Linscheid, M.D.
10:20 A.M.	Use of the Zickel Nail in Peritrochanteric Hip Fractures—Elmer Lippmann, Jr. M.D.
10:40 A.M.	Total Joint Replacement of the Hip and Knee: Indications and Current Thinking on Patient Selection.—R. Wynn Kearney, Jr. M.D.
11:00 A.M.	Uses of Isoenzymes in Clinical Medicine—J. B. Crespo, M.D.
11:20 A.M.	Unusual Clinical Manifestations of Primary Hyperparathyroidism—Donald A. Scholz, M.D.
11:40 A.M.	Mammography, Xeromammography and Thermography—Comparative Values—John J. Gisvold
1:30 P.M.	Is Coronary Artery Disease a Surgical Problem?—Richard C Lillehei, M.D.
1:50 P.M.	Too Fat to Breathe—Norman G. Hepper, M.D.
2:10 P.M.	Non Seroidal Anti-Inflammatory Drugs in Treatment of Rheumatoid Arthritis—R. B. Tompkins, M.D.
2:30 P.M.	Cancer of the Paranasal Sinuses—Bruce W. Pearson, M.D.
2:40 P.M.	Current Status of Total Parenteral Nutrition in Infants and Children—Robert Telander, M.D.

Physicians Take Note

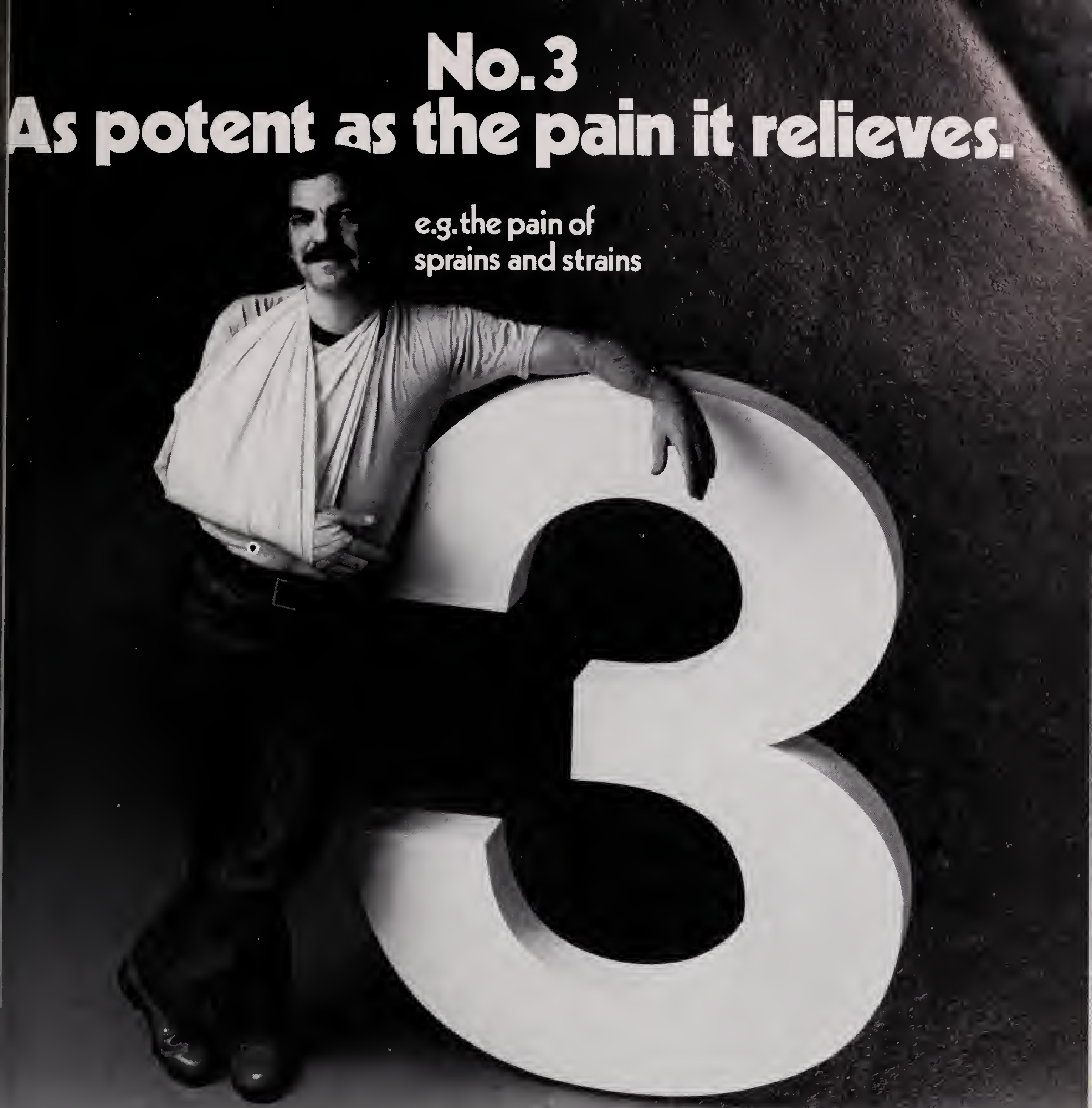
Dispense as Written (DAW) Needed on Prescriptions to Preclude Substitution

Physicians are reminded that the 1975 Legislature enacted a new law, Chapter 101, authorizing generic drug substitution under certain conditions. Responding to this new legislation the 1975 AMA House of Delegates passed the following resolution:

"Physicians are again urged to write 'Dispense as Written' or 'D.A.W.' (this must be written in the physician's handwriting) on a prescription when in the physician's professional judgment the patient's health and welfare might be compromised by the substitution of another medication for that which he has specifically identified on his prescription."

The law provides that a pharmacist who receives a prescription for a brand name drug, may, with written or verbal consent of the purchaser, dispense any drug generically equivalent to the brand name prescribed unless the above procedure is followed.

Chester A. Anderson, M.D.
Chairman
Legislative Committee



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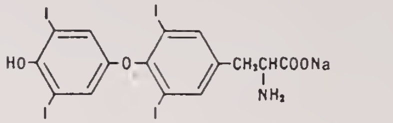

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Both SYNTHROID products will provide L-thyroxine as a substrate for physiologic deiodination to L-triiodothyronine. Therefore, patients taking SYNTHROID products will demonstrate normal blood levels of L-triiodothyronine even when the thyroid gland has been surgically removed or destroyed by radioiodine. Administration of levothyroxine alone will result in complete physiologic thyroid replacement.

Indications: SYNTHROID (sodium levothyroxine) products serve as specific replacement therapy for reduced or absent thyroid function of any etiology. SYNTHROID **Injection** can be used intravenously whenever a rapid onset of effect is critical, and either intravenously or intramuscularly in hypothyroid patients whenever the oral route is precluded for long periods of time.

Contraindications: There are no absolute contraindications to SYNTHROID (sodium levothyroxine) therapy Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis (See WARNINGS)

Warnings: Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated. Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met Clinical judgment will then dictate either a less-than-complete restoration of thyroid status or reduction in thyroid dosage.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. SYNTHROID (sodium levothyroxine) therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

Precautions: Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule With SYNTHROID (sodium levothyroxine) **Tablets,** the relatively slow onset of action minimizes the risk of overdose but close observation in the weeks following institution of a dosage regimen is advised. Treatment of thyroid hyperactivity induced by oral medication is confined to interruption of therapy for a week, followed by reinstitution of daily therapy at an appropriately reduced dosage.

Adverse reactions: Adverse reactions are due to overdose and are those of induced hyperthyroidism.

Dosage and administration: For most adults, a final dosage of 100 mcg (0.1 mg) to 200 mcg (0.2 mg) of SYNTHROID (sodium levothyroxine) **Tablets** daily will restore normal thyroid function and only occasionally will patients require larger doses. Failure to respond adequately to a daily oral intake of 400 mcg (0.4 mg) or more is rare and should prompt reconsideration of the diagnosis of hypothyroidism, special investigation of the patient in terms of malabsorption of L-thyroxine from the gastrointestinal tract or poor adherence to therapy.

The concomitant appearance of other diseases, especially cardiovascular diseases, usually dictates a replacement regimen with initial doses smaller than 100 mcg/day (0.1 mg).

In otherwise healthy adults with relatively recent on of hypothyroidism, full replacement dose of 150 mc (0.15 mg) or 200 mcg (0.2 mg) has been instituted immediately without untoward effect and with good therapeutic response. General experience, however, favors a more cautious approach in view c the possible presence of subclinical disorders of the cardiovascular system or endocrinopathies.

The age and general physical condition of the patie as well as the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. In the elderly patient with long standing disease, evidence of myxedemato infiltration and symptomatic, functional or electrocardiographic evidence of cardiovascular dysfunction, the starting dose may be as little as 25 mc (0.025 mg) per day. Further incremental increases of 25 mcg (0.025 mg) per day may be instituted at thr to four week intervals depending on patient response. Conversely, otherwise healthy adults may be started at higher daily dosage and raised to the full replacement dosage in two to three weeks. Clearly it is the physician's judgment of the severity of the disease and close observation of patient response which determines the rate of dosage titration.

Laboratory tests to monitor thyroid replacement therapy are of limited value. Although measurement of normal blood levels of thyroxine in patients on replacement regimens frequently coincides with th clinical impression of normal thyroid status, higher than normal levels on oral replacement of levothyroxine occasionally occur and should not be considered evidence of overdosage per se.

In all cases, clinical impression of the well-being of the patient takes precedence over laboratory determination in determining the appropriate individual dosage.

In infants and children, there is a great urgency to achieve full thyroid replacement because of the critica importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body size, the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult, as much as 300 mcg (0.3 mg) to 400 mcg (0.4 mg) per day.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of SYNTHROID **Injection** may be administered intravenously as a solution containing 100 mcg/ml. Although the patient may show evidence of increased responsivity within six to eight hours, full therapeutic effect may not be evident until the following day An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvement has not occurred. Like the oral dosage form, SYNTHROID **Injection** produces a predictable increase in the circulating level of hormone with a long half-time. This usually precludes the need for multiple injections but continued daily administration of lesser amounts intravenously should be maintained until the patient is fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine intravenously is clearly not without its cardiovascular risks. Under such circumstances, intravenous therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgment in this situation may dictate smaller intravenous doses of levothyroxine.

SYNTHROID **Injection** by intravenous or intramuscular routes can be substituted for the oral dosage form when ingestion of SYNTHROID **Tablets** is precluded for long periods of time.

How Supplied: SYNTHROID (sodium levothyroxine) **Tablets** are supplied as scored, color-coded compressed tablets in 6 concentrations: 25 mcg (0.025 mg)—orange . . . 50 mcg (0.05 mg)—white . . . 100 mcg (0.1 mg)—yellow . . . 150 mcg (0.15 mg)—blue . . . 200 mcg (0.2 mg)—pink . . 300 mcg (0.3 mg)—green.

SYNTHROID (sodium levothyroxine) for **Injection** is supplied in 10 ml vials containing 500 mcg of lyophilized active ingredient and 10 mg of Mannitol, U.S.P. A separate 5 ml vial containing Sodium Chloride Injection, U.S.P is provided as a diluent.

Directions for reconstitution: Reconstitute the lyophilized sodium levothyroxine by aseptically adding 5 ml of the Sodium Chloride Injection, U.S.P. to the vial. Shake vial to insure complete mixing **Use Immediately** after reconstitution. Discard any unused portion.

U.S. Pat. 2,889,363

January 1975

Editorials

Assessment of Gestational Age

McDonald and Fish elsewhere in this issue comprehensively discuss the prenatal assessment of intrauterine growth retardation. They correctly point out that infants with a birth weight of less than 2500 grams account for 75% of all neonatal deaths. Those infants also are at increased risk for cerebral palsy and other adverse neurologic sequelae.

A very important factor in assessing infant mortality risk is gestational age, since it has been shown that for any constant birth weight the mortality rate decreases as gestational age increases. The importance of determining the gestational age is emphasized by a detailed discussion of the techniques that have been developed to estimate the duration of pregnancy. The clinical observations such as the date of the last menstrual period and Naegele's rule, estimation of uterine size by palpation or measurement, the dates of quickening and engagement of the fetal head and auscultation of the fetal heart tones with the head stethoscope all have inherent inaccuracies well known to every obstetrician. The interpretation of the biochemical and biophysical methods such as estriol, ultrasound, and phospholipids are more parameters of fetal well being or growth retardation rather than an accurate measurement of gestational age.

In high risk pregnancy complicated by medical problems such as diabetes, hypertension, renal disease, and a whole host of other less common maternal conditions, the obstetrician, generalist or internist who is aware of the maternal condition should caution the individual to seek preconceptional consultation to establish full awareness of the hazard of the maternal condition to the well being of the fetus, and convey to her the importance of knowing at all time during pregnancy the exact duration of gestation. To insure this, *those* women who are contemplating pregnancy should be instructed in the potential value of the basal body temperature graph to determine the exact date of conception. Not only will this knowledge be invaluable for the high risk pregnancy, but it will be invaluable if the pregnancy is complicated by toxemia, placenta previa, or other unanticipated complications resulting from the pregnancy itself.

Because ovulation may be delayed or occur erratically in the first cycles after discontinuance of oral contraceptive pills, every woman who discontinues this medication to become pregnant should be instructed in basal body temperature recording to identify the time of ovulation and hence the date of conception.

Konald Prem, M.D.
Minneapolis, Minnesota

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*See page 609.

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Medical Compliance

The Effect of Appointment Reminders on Keeping Appointments in a Core City Pediatric Outpatient Department

WILLIAM MELLER* and ARNOLD ANDERSON, M.D.†

A study of medical compliance in a racially mixed low socio-economic patient population at Minneapolis Children's Hospital used postal reminder cards, transportation option sheets, and increased staff enthusiasm. Postal reminder cards were found to significantly increase compliance among those receiving the cards.

THE TOPIC "MEDICAL COMPLIANCE" refers to a patient's willingness to follow the directions of a physician or other qualified personnel. One important aspect of medical compliance is appointment-keeping. The purpose of this paper is to demonstrate that in a core city outpatient department the appointment-kept rate can be significantly improved by simple and inexpensive methods.

There are three complementary methods for improving the appointment kept rate which have been effective in a variety of clinical settings: (1) postal appointment reminder cards, (2) education regarding convenient transportation arrangements to and from the hospital, and (3) increasing staff enthusiasm. Postal reminder cards, post cards mailed about a week before the appointment, listing the date, time and place, have been found to cut the broken appointment rate by as much as 50%. Mailing is more effective than telephoning because of its potential to contact larger numbers of people; many patients do not have telephones or are not at home to answer them.[1-3] Handouts showing convenient routes to take and times to go to the clinic increased the compliance rate in a university health service.[4] Staff enthusiasm has also been pointed to as being important to compliance.[3] These three methods were combined at Children's Hospital of Minneapolis and the following paper is a discussion of their effect on appointment-keeping.

Patient Population

The patient population at Minneapolis Children's is ideal for the study of compliance. The hospital is located in a low socio-economic neighborhood and is concerned with individuals up to age 16. Thus, the compliance problems associated with a lower socio-economic patient clientele along with all of the problems inherent in a pediatric clinic are encountered. Pediatric clinics are second only to those in mental health in their poor compliance rates.[5] Thirty-four percent of the patients at the Minneapolis Children's Hospital outpatient department are non-white; of these 82.39% are Black and 14.7% are American Indian. Non-white cultural groups often do not hold the traditional view of the doctor as an authority figure to be trusted.[6] For this and other reasons, non-whites have a much lower rate of compliance.[7,8,3]

Over 60% of the patients using the pediatric outpatient department at Minneapolis Children's are on welfare. Hutardo points out that "the medically indigent have a significantly higher rate of appointment failures which suggests that studies of appointment failures, when dealing with medically indigent populations, may have limited pertinence to other population groups."[5] This view should be kept in mind throughout the reading of this paper.

Procedure

Postal appointment reminder cards were sent out by two volunteers. The cards were mailed enough in advance so that they would reach the

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*Carleton Student—paper was a project for sociology course.
†Pediatrician, Children's Health Center of Minneapolis.

We would like to thank Niel Lutsky, Instructor in Psychology, Carleton College, and Bonnie Totino of Minneapolis Children's Hospital for their help with this paper.

patient two to five days before the scheduled appointment. Also, a list of free or inexpensive transportation options which would be convenient for most Children's Hospital patients was made available at the hospital.

To create an enthusiastic attitude towards compliance among the staff, a special presentation of a brief review of the literature on compliance with compliance statistics of the hospital was given to the entire outpatient department staff. Written copies were then distributed to various staff members.

Results

The postal reminder cards were sent to a sample of 566 patients from February 26 to May 9, 1975. The average broken appointment rate for one year previous to this time had been 28.4%. During the target months of March and April, the broken appointment rate of the sample which received the cards was 16.97%. The difference here is significant. (chi-square = 25.2 p 0.01). Of the patients who made appointments during the two month target period, only 33.96% received postal reminder cards. The 66.04% of the patients who did not receive postal reminder cards had a 30.9% non-compliance rate as compared with a 16.97% rate for those who did. (chi-square = 27.9 p 50.01).

Although it is impossible to determine quantitatively the effects of the transportation option sheets on compliance, we have received positive verbal response to them. 1200 sheets were taken by patients and more were requested.

Increased staff enthusiasm has generated new ideas on ways to deal with the problem of high broken appointment rates. Ideas such as asking mothers to address their own appointment cards, explaining the financing more clearly to the patients, and having the medical residents play a more active role in appointment follow-up, were discussed by the staff.

Discussion

A 15% broken appointment rate is viewed as the optimum target to which a clinic can reasonably aim.[3] The Minneapolis Children's outpatient department has closely approached this goal in the target months sample which received cards (16.97%). Although this represents a highly significant decrease from the hospital's average rate, such a low percentage of the patients was reached by the reminder cards that the target months total compliance rate did not decrease as significantly as we expected. This points out the most important problem facing this study—getting the reminder cards to the patients. One possible solution will be discussed later.

The compliance rate of the patients who did not receive cards during the target months did not increase; thus, the added staff enthusiasm hopefully generated through education had a limited effect on the appointment-kept rate. No conclusions can be drawn about the transportation option sheets as they did not become available until the last half of the target period.

The postal reminder card has proven to be a very effective and inexpensive method for decreasing the broken appointment rate. The cost of buying and mailing these 566 cards was under $80.00. By increasing the number of appointments kept and thereby minimizing the number of wasted time slots in which the doctor had planned to see a patient but did not, the appointment cards saved the hospital many times this amount.

How can the system of mailing appointment cards be improved? Ideally, every patient who makes an appointment should receive a card. One way to accomplish this is to ask the mother to address the reminder card at the time the return appointment is made. This method eliminates the problems of improper addressing, and helps the mother feel supportive to the staff, an important aspect of a child's health care. When patients make appointments by telephone, cards are addressed by staff members.

Conclusion

Medical compliance is an important aspect of health care, especially in certain patient populations. There are three methods for improving the appointment-kept rate: postal reminder cards, transportation option sheets, and increased staff enthusiasm. Postal reminder cards are an effective method to improve appointment-kept rates. A system of mailing reminder cards which includes participation by the mothers has been suggested.

References

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3-8. Will be found on page 659.

President's Address

I am interested in issues and problem solving. I want to be inventive, creative—in essence, outplan the planners.

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1. The right of the patient to choose the physician and hospital of his or her choice.
2. The right of the patient to privacy.
3. The right of the patient to be protected from exploitation.
4. The right of the physician to practice in the medical specialty and location of his choosing.
5. The right of the physician to exercise his judgment in the art and science of medicine without interference from third parties.
6. The right of the physician to be judged by his peers and to be disciplined by his peers.

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Division Socio-Economic and Legislative Affairs.

Malpractice

NEED TO LOOK AT OUR OWN EXPERIENCE WITH VOLUNTARY BINDING ARBITRATION AND THE EXPERIENCE IN MICHIGAN. WE NEED TO RE-INTRODUCE OUR OWN FIVE OR SIX BILLS IN THE NEXT LEGISLATIVE SESSION. BUT MOST IMPORTANT FOR THE NEXT YEAR—I PROPOSE AND WILL ASK THE CHAIRMAN OF THE COUNCIL TO APPOINT AN AD HOC COMMITTEE TO STUDY THE FEASIBILITY OF SELF INSURANCE BASED ON THE ILLINOIS EXPERIENCE. ET AL.

Formation Division Public Relations

PSRO—The intent of the law as passed by Congress has been changed as it has been implemented by HEW. The AMA has submitted 19 amendments to the existing law in an attempt to correct the original intent. They have successfully obtained passage of three of them including postponing the authority for the secretary of HEW to enter into PSRO contracts with groups other than professional associations until July 1, 1978. The sixteen remaining amendments include such vital issues as:

Confidentiality of data.

Guidelines (referring to norms, criteria and standards) are to be guides only and cannot be substituted for individual professional judgment with *local authority and variation* paramount in developing these guidelines.

HMO—

S 1926 HMO Amendments of 1975

Basically this law seeks a substantial reduction in what are now considered to be basic health services provided under the HMO law. It is true that this reduction would *result in lower costs for HMO operation* and this would seem to be an admirable objective. However, there is another side to this two edged sword. The *important point* here is that while the reduction of these services should have a cost saving benefit, the HMO is no longer in a *competitive* position—if it ever really was—with other physician health care provider group systems.

If the intent is to prove that an HMO is less costly than physician health care outside the HMO framework, then the reduction in these essential services will probably prove this point.

Many of the provisions in those amendments are designed to create a more attractive environment for the HMO. For example, the elimination of "open enrollment" creates a situation where an HMO is protected from accepting patients who are likely to demand many services because of their health.

To remove coverage of dental care for children, care of chemical dependency, care of mental illness, etc. from the basic coverage in HMO insurance plans brings a disservice to members enrolled in such HMOs and provides those HMOs with a competitive edge over other forms of medical practice which are providing full services.

Given before the House of Delegates, May 21, 1976, during the Annual Meeting of the Minnesota State Medical Association in Rochester.

Health Professionals Education Assistance Act
Gone to Full Committee Senate

The existing law has been extended through fiscal year 1977. There are several proposals in the new law which would have great impact on medical schools, students, residents, and physicians in private practice. The findings and purpose of the act *states the fact* that the quality and availability of health care in the U.S. affects interstate commerce and; justifies programs of obligated service by health professions, certification of post graduate physician training programs, and development of minimal standards for the licensure and re-licensure of physicians and dentists. Some areas of concern:

1. Student assistance loans will be replaced by a new program of federally insured loans.
2. Post graduate physician training programs would be regulated as to the number and kind.
3. Model standards for re-licensure every six years will be developed for practicing physicians.
4. Capitation grants to medical schools per student will be given if there is assurance that 35% of the first year students have agreed to accept NHSC Scholarships and that by 1980, 50% of filled residencies be in family practice, primary internal medicine and primary pediatrics.

IF WE *BELIEVE* THAT THE *WELFARE* OF THE SICK IN AMERICA CAN BEST BE SERVED BY COMPETENT PHYSICIANS—*MOTIVATED* BY DEDICATION TO SERVICE—AND WITH AN *ABILITY TO SUCCEED* IN THEIR CHOSEN PROFESSION, BY THEIR *OWN EFFORTS,* IN A PRIVATE SETTING—THEN IT BEHOOVES EACH OF US THRU INDIVIDUAL EFFORT TO PARTICIPATE IN THE *DECISION MAKING PROCESS*—BECOME DIRECTLY INVOLVED IN SOLVING THE MANY ISSUES OF OUR TIME. WE CAN ONLY ACCOMPLISH THIS THRU OUR *PRESENCE,* OUR *UNITY,* OUR OWN *INNOVATIVE PROGRAMS* AND OUR *STRENGTH.* WE THEN MUST GET THE MESSAGE TO THE PEOPLE.

Richard E. Anonsen, M.D.
President

BOOK REVIEW

WORK AND FATIGUE: Psychological Aspects and Physiological Correlates. By Ernst Simonson and Philip C. Weiser. Charles C. Thomas. Springfield, IL. 1976. pp 445. $39.50.

"Work and Fatigue" was projected to be the mid-portion of a trilogy of which the first volume "Physiology of Work Capacity and Fatigue" appeared in 1971.

Simonson's death in 1975 leaves the final volume "Exercise and Fatigue in Disease" for others to complete, and, in the words of Simonson's good friend and collaborator, Josef Brozek, thus brings to completion Ernst's grand design. Twelve contributors joined the editors completing the six sections: Physiological Background, Motor Aspects, Vision, Central Processing, Aging and Introspective Aspects of Work and Fatigue.

Hans Schaefer, the German physiologist, in an Epilogue states: "Fatigue is one of the most exciting and most mysterious phenomenon profoundly affecting our very existence, as any reader can tell when he attempts to integrate the multifaceted aspects of fatigue presented in this book. Fatigue decides the outcome of our endeavors; success or failure, achievement or resignation, alertness or submergence in sleep or forgetfulness. Fatigue is the key for understanding the genius whose distinction often consists largely in an extraordinary memory and nearly absent fatiguability." (I think Schaefer had Ernst in mind as an illustration of such a person.) Simonson had a lifelong interest in fatigue and published extensively in this area. In addition to his native Germany he has worked in Russia, Czechoslovakia, and finally in the United States in Milwaukee and Minneapolis. These books undoubtedly will serve as the standard reference on Fatigue for many years to come.

Reuben Berman, M.D.
Editor Emeritus

MSMA Highlights

MINNPAC

By now everyone knows 1976 is an election year. As such, the Minnesota Medical Political Action Committee or MINNPAC is again reviewing the federal and state election races and choosing candidates to support.

Each year, the MINNPAC selections create some misunderstanding. With this in mind, this article briefly details how we choose to support certain candidates, and the reason for our choices.

In 1975, MINNPAC sent a questionnaire to all Minnesota physicians. We asked them a variety of questions that would help the MINNPAC Board determine the direction of our 1976 activities. To review a few of our findings:

(a) 80% of the physicians lean or are Republicans, but 70% responded that political affiliation is not important in determining candidate support,
(b) Most physicians felt it was more important for a candidate to "be favorably disposed toward medicine" than to be "expected to win," and
(c) 68% believed if we contribute to a candidate, that candidate will more readily listen to our opinions (20% were undecided).

One statistic disturbed us: 51% said they didn't know who MINNPAC contributed to or why. This is another reason for this article.

We were determined to employ sound statistical analysis for the 1976 races hopefully to avoid as much bias as possible. We attempted to discover voting trends in each legislative district.

We began by calculating a partisan index for each of the 201 legislative districts (Senate and House). Such things as past party preference, ballot placement, Watergate effect, and "coattails" (Humphrey's and Mondale's) were researched. Each race was then given a "normative party strength rating."

Next we ranked the races using such factors as incumbency, voter turnout and if the seat was "open" or not. These calculations gave us an objective basis to begin our candidate review.

A Candidate Review Committee was then established, selected from the members of the MINNPAC Board of Directors. (Each County Society has an opportunity for representation on the Board, although certain societies have not designated appointees.) Care was taken to get a good political and geographic mix to assure fairness.

This Candidate Review Committee met after filings closed on July 20th. It was this group that inserted the subjective factors into our decisions: candidate strength, past effectiveness, legislative performance, and campaign potential. These were reviewed, and candidates were chosen for support.

Each race was ranked "1," "2," or "3," with "1" being the highest level of support. After these were designated, dollar levels were assigned to each number. Generally for the House, this means $300, $200, and $100 and for the Senate, $500, $300, and $100 respectively.

After another review these decisions were then ratified by the Board of Directors. Our initial decisions were not final, however. As everyone in politics knows, a lot can happen between July and November. The Presidential race will have an effect, as will Congressional races. We have yet to weigh the effect of the primary election on September 14th. What this all means is that the MINNPAC Board may need to make additions and subtractions to our list. Levels of support may vary, as will the priorities medicine places on our selections.

To aid in this process, we will need continual information. We will be traveling throughout the state interviewing candidates and local physicians for input.

The current political make-up in the State Senate is: 38 Democrats, 28 Republicans, and one Independent. In the House it is: 103 Democrats and 31 Republicans. Recognizing these political realities, and that 70% of our physicians believe political affiliation is not important, we carefully reviewed each race.

For the record, our preliminary decisions of support are as follows:

State Senate:
22 Democrats and 24 Republicans
State House:
39 Democrats and 34 Republicans

Again, these totals will change. If you have any information or just wish to know about your area, please give us a call, MINNPAC is *your* organization. We seek to help medicine, and that can only be done when everyone works to support candidates who are understanding and objective about medicine's socio-economic problems in Minnesota. MINNPAC is effective, but much more so when MINNPAC has your support.

One way you can demonstrate that support is by joining MINNPAC and AMPAC if you have not already done so for 1976. Your annual dues of $50 should be sent to: MINNPAC, P.O. Box 30292, St. Paul, MN 55165.

An important additional step would be your support of the candidates of your choice running for the State Legislature and Congress.

Remember, to a large degree, the future of our profession will be determined by these legislative bodies, the make-up of which we help determine.

Richard Engwall, M.D.
Chairman, MINNPAC

A copy of our report is filed with the appropriate offices is available for purchase from the Superintendent of Documents, United States Government Printing Office, Washington, D.C. 20402.

Annual Meeting

Make an Appointment with DOC

Where? At the beautiful Radisson South Hotel, Bloomington. So mark your calendar for May 19 and 20 and prepare to attend the best MSMA Annual Meeting ever!

"Doctors' Office Call" is the theme for the '77 Annual Meeting. Abbreviated, its spells DOC, but that's where the brevity ends. From the first rap of the gavel at the House of Delegates to the last adieu on Friday, Annual Meeting 1977 is abundant with activities to interest everyone. Once again, the seminar format will be used to present enlightening, accredited scientific sessions. You'll enjoy learning in the Radisson's spacious and comfortable Veranda Rooms, convenient to Meeting registration, exhibits and relaxation. If more strenuous relaxation is your style, why not display it at the Meeting's tennis or golf tournaments. Thursday, the President's Reception and Annual Banquet featuring an evening of entertainment and dancing will be held in the grandeur of the Great Hall. But, please save one waltz and join us Friday for an "Afternoon in Vienna" where we'll conclude the Meeting in relaxing three-quarter time.

The theme, "Doctors' Office Call," will flavor the content of most scientific sessions and makes possible an eclectic program applicable to *your* daily practice. Seminars will concentrate on subjects dealing with in-office problems and concerns including topics varying from financial planning and office management to office pediatrics and office psychiatry. The enthusiasm of this year's Scientific Assembly Subcommittee coupled with excellent meeting facilities is certain to make DOC an unforgettable learning experience for Minnesota physicians.

Educationally, socially, politically—DOC has it all for you. Plan now to keep your appointment with DOC May 19 and 20, 1977.

R. D. Semsch, M.D.
Chairman
Scientific Assembly Subcommittee

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CONSERVES POTASSIUM

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

* Warning
This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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RIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

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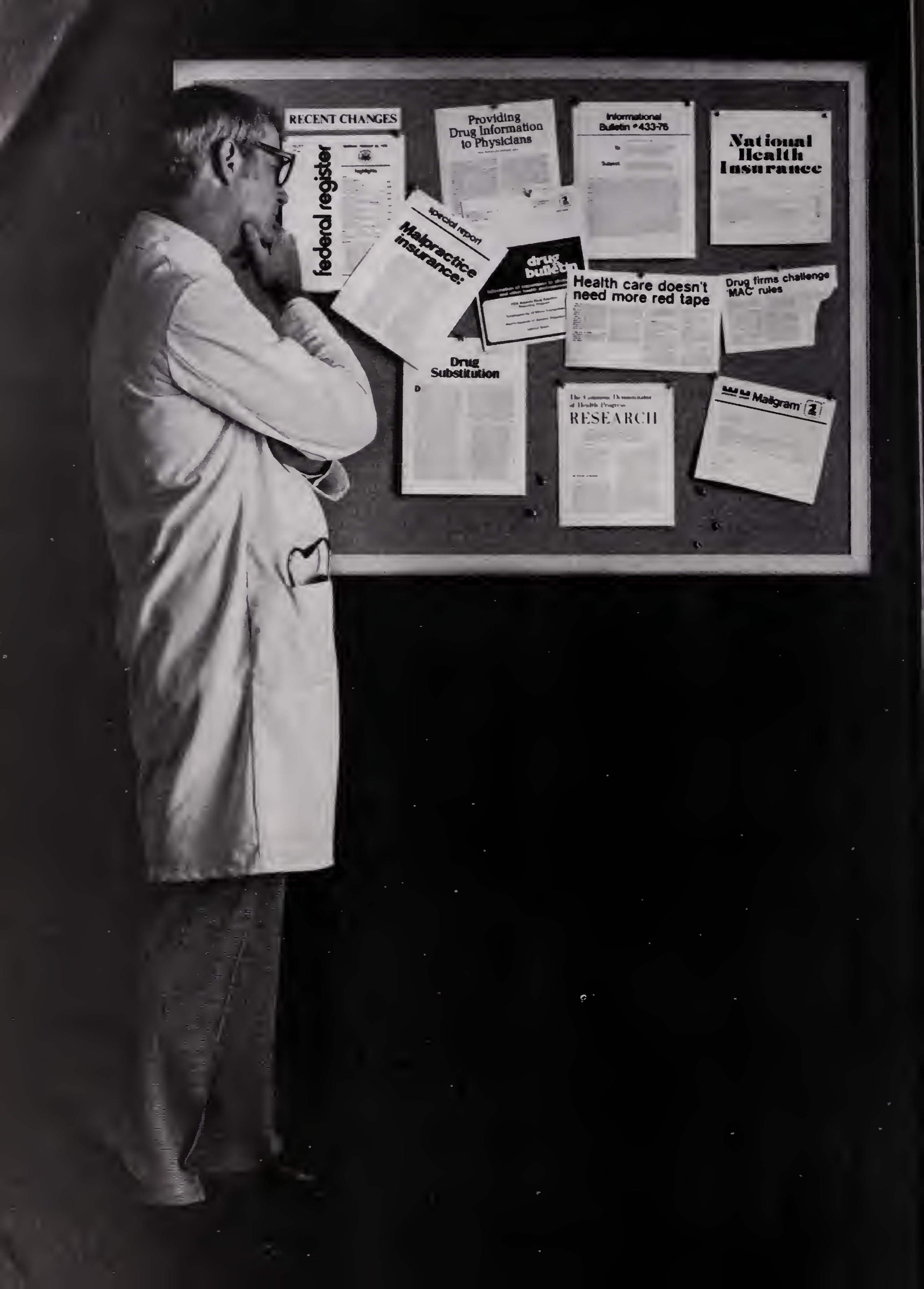
New York New York 10017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Health care doesn't need more red tape
Drug firms challenge 'MAC' rules
Drug Substitution
RESEARCH
Mailgram 2

THERE ARE A LOT OF PEOPLE GETTING BETWEEN YOU AND YOUR PATIENT.

Medicine today is in the spotlight, subjected to all nds of scrutiny. Your control over patient therapy is ing monitored, judged and occasionally abrogated, metimes by unknown third parties.

The worry is that in the wake of this focus, the rela- onship between you and your patient will be weakened, ithout offsetting benefits. Consider three examples:

Drug substitution In most states, pharmacy laws, gulations or professional custom stipulate that your n-generic prescriptions be filled with the precise prod- ts you prescribe. But in the last five years, a dozen or ore State laws have been changed, permitting the phar- acist in most cases to select a product of the same neric drug to fill any prescription.

Ironically, this dilution of physician control has ken place against a background of growing evidence at purportedly equivalent drug products may be in- uivalent, since neither present drug standards nor their forcement are optimal. In fact, the FDA itself says it s not enforced the same standards for hundreds of ollow-on" products that it had applied to the original DA approvals. Thus physician control over patient erapy is being eroded with a risk that patients may be posed to drugs of uncertain quality.

The major advertised claim for substitution is reduced escription prices for consumers. Yet no documentation any significant savings has been produced.

MAC Maximum Allowable Cost, MAC for short, is ederal regulation designed to cut the Government's ig bill by setting price ceilings for drugs dispensed to edicare and Medicaid patients. Unless the prescriber rtifies on the prescription that a particular product is edically necessary, the Government intends to pay only the cost of the lowest-priced, purportedly-equivalent, generally-available product. The effect of the program may be that elderly and indigent patients will be restricted to products which someone in Washington believes are priced right. Practicing doctors will have little to say about administration of the program, since Government will have absolute authority to make its choices stick.

The drug lag The future of drug and device research depends upon a scientific and regulatory environment that encourages therapeutic innovations. The American pharmaceutical industry annually is spending more than $1 billion of its own funds and evaluating more than 1,200 investigational compounds in clinical research. Disease targets include cancer, atherosclerosis, viruses and central nervous system disorders, among others. But there is a major barrier to the flow of new drugs to your patients: The cost of the research is more than ten times what it was, per product, in 1962; and whereas governmental clearance of new drug applications took six months then, it commonly consumes two years now.

The FDA needs adequate time, of course, to consider data. But it is equally clear that the present approval process contributes to needless delay of needed therapy. That's why the increased efficiency of the drug approval process is vital to all our futures.

If these issues concern you, we suggest that you make your voice heard—among your colleagues and your representatives in State legislatures and in Washington.

It could make a difference in your practice tomorrow.

P·M·A

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WANTED—CHILD PSYCHIATRIST or Psychiatrist to join a well established four man group located in University community of 46,000 with a large referral area. We have two excellent hospitals. Community is 90 miles from Twin Cities. Salary is open. For further information contact E. R. Brousseau, M.D., Northwest Psychiatric Clinic, Eau Claire, Wisconsin 54701. Telephone: 715-834-2751.

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OPPORTUNITIES AVAILABLE—Family Practitioner and Surgeon—beautiful community of Elbow Lake, Minnesota, population 2000 with drawing community of 7000. Modern 32 bed hospital. Contact Ward A. Stoddard, telephone 218-685-4461 or write.

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ANESTHESIOLOGIST—Board certified/eligible, immediate opening, exceptional opportunity, replacement of retiring Anesthesiologist. New highly modern and actively expanding 109 bed Waconia Ridgeview Hospital, located in metropolitan 7 counties, 30 miles S.W. of Minneapolis in beautiful Carver County. Active medical staff of 30 specialist and family practitioners. Outstanding growth potential. Write: Executive Director, Waconia Ridgeview Hospital, 500 South Maple Street, Waconia, Minnesota 55387. Call: Area Code 612, 442-2191.

EDINA—Opportunity for a family physician to join an established corporate group of seven physicians. Group currently consists of six family physicians and one general surgeon. Clinic is located approximately one quarter mile from a 450 bed hospital. Contact J. Turonie, Administrator at 612-920-5966.

INTERNIST to join progressive five-man group. Central Minnesota. 130 bed hospital. Lake area. Starting salary $40,000 per year. Fantastic practice opportunity. Contact Little Falls Clinic, Little Falls, Minnesota. 612-632-5305.

WANTED—Family practitioner, board eligible or board certified, to join 10-man multiple-specialty group with emphasis on family practice. Group now consists of seven family practitioners, one surgeon, one internist and two associates in OB-GYN. Located 30 miles west of Minneapolis, in brand new clinic facilities fully equipped for 12-man group next to 105-bed, fully accredited by JACH, designated area hospital. Contact J. W. Clarke, M.D. 448-2323.

(Continued to page 660)

Special Article

Pathology of the Myxomatous Mitral Valve[*]

Nature, Secondary Changes and Complications

RICHARD B. GUTHRIE, M.D.[†] and JESSE E. EDWARDS, M.D.[†]

MYXOMATOUS DEGENERATION, change or transformation of the mitral valve is now recognized as a fairly common condition although the first description of it as an entity is only a decade old.[1] This change has been correlated with an unduly lax nature of the leaflets and chordae yielding such clinical findings as "mid-late" or late systolic click and late or pansystolic murmurs.[2] Each of the foregoing has been associated with echocardiographic and angiocardiographic signs of prolapse or overshooting of the mitral leaflet tissue toward the left atrium.[3-5] This process has been variously called prolapse,[6,7] billowing,[8] ballooning or hooding of the mitral valve and floppy mitral valve.[9] It may be observed both in subjects with arachnodactyly (Marfan's syndrome)[10] and in subjects without this condition.[11,12]

The pathologic changes in involved mitral valves are characteristic, although some of these have been confused with the end results of rheumatic endocarditis[12] or of healed bacterial endocarditis. Also, "spontaneous" rupture of chordae, which appears to be one of the complications of myxomatous change of the mitral valve, has

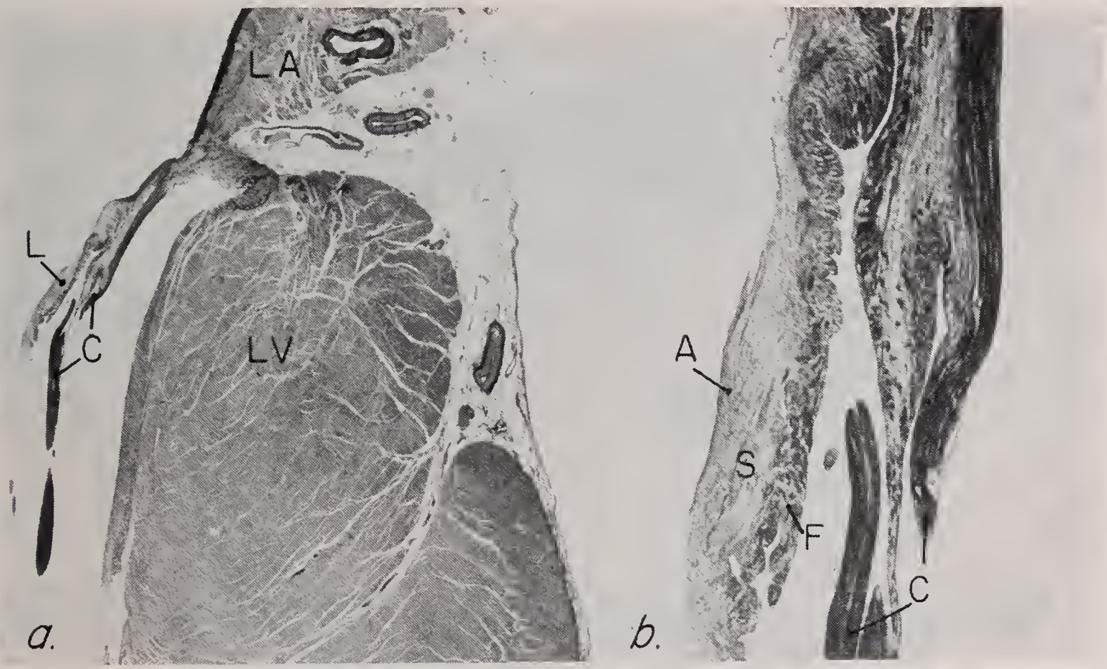

Fig. 1—Photomicrographs of normal mitral valve. (a) Low power view of left atrium (LA) and left ventricle (LV), as well as the posterior mitral leaflet (L). Chordae (C) extend to the leaflet. Characteristically, the leaflet is thin. Elastic tissue stain; x 3.8 (b). Segment of leaflet shown in (a). The leaflet is composed of the following layers: auricularis (A), spongiosa (S), and fibrosa (F). Chordae are indicated by letter. C. Elastic tissue stain; x 20.

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[*] Presented at Grand Rounds, Department of Laboratory Medicine and Pathology, University of Minnesota, March 31, 1976.

[†] Departments of Pathology, United Hospitals-Miller Division, St. Paul, Minnesota and the University of Minnesota, Minneapolis, Minnesota, and from the Department of Internal Medicine, United Hospitals-Miller Division.

This study was supported by Public Health Service Research Grant 5 RO1 HL05694 and Research Training Grant 5 TO1 HL05570 from the National Heart, Lung and Blood Institute, and by grants from the Bremer Foundation and The Saint Paul Foundation, St. Paul, Minnesota.

not consistently been so identified as it has, by some, been considered as a self contained entity.

The basis for certain pathologic misinterpretations of the various ramifications of myxomatous change of the mitral valve stems from lack of a detailed description of the secondary changes and complications of the myxomatous mitral valve. Most reports, with few exceptions,[13-15] dealing with the histologic nature of the mitral valve involved by myxomatous change have stressed the phenomena of myxomatous change and "fibrosis" without defining the specific locations at which fibrosis occurs.

It is the purpose of this report to describe the primary histologic nature of myxomatous change of the mitral valve and the secondary changes which follow as reactions to the altered hemodynamics of this condition.

The secondary changes include characteristic fibrous deposits upon the valve leaflets and chordae, as well as fibrous lesions involving the left ventricular mural endocardium.

Reference will be made to complications of the myxomatous mitral valve which include rupture of chordae tendineae, bacterial endocarditis and calcification of the valvular tissue.

Normal Mitral Valve

Gross and Kugel[16] described the normal mitral leaflets as being composed of four layers as follows: (1) the auricularis, (2) the fibrosa, (3) the ventricularis and (4) the spongiosa (Figure 1).

The *auricularis* is a thin layer composed of collagen and elastic tissue forming the contact or atrial aspect of the leaflet. This layer is continuous with the endocardium of the overlying atrium. The *fibrosa* forms the basic support of the leaflet and is composed of dense layers of collagen. This layer which, on one hand, is a continuation of the fibrous tissue of the annulus (in the case of the posterior leaflet) or the aortic-mitral intervalvular fibrosa (in the case of the anterior leaflet) is, on the other hand, continuous with the chordae tendineae. The latter are also formed by dense collagen. The third layer, the *ventricularis,* covers the ventricular aspect of the fibrosa and is continuous in the case of the posterior leaflet with the endocardium of the left ventricle. The fourth layer, namely the *spongiosa,* lies between the auricularis and fibrosa layers. The spongiosa is formed by delicate myxomatous connective tissue. Since the ventricularis is a thin layer and tends to disappear toward the free

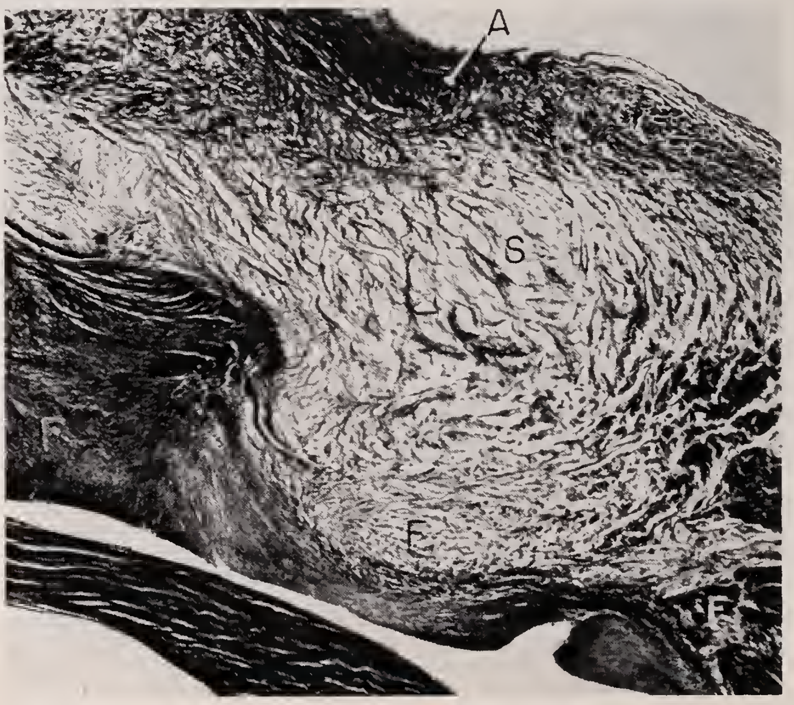

Fig. 2—Myxomatous mitral valve. The spongiosa (S) is voluminous and encroaches upon both the fibrosa (F) and the auricularis (A). Elastic tissue stain; x 40.

end of the leaflet, it will be considered as part of the fibrosa in this report.

Myxomatous Change

Valves involved by myxomatous change, in addition to exhibiting the primary process, frequently show secondary changes, as well. The latter include fibrous proliferation in various locations, the fibrotic proliferation leading at times to confusion with other conditions, such as chronic rheumatic endocarditis or healed bacterial endocarditis.

Primary Process

As the spongiosa layer of normal mitral valves varies in thickness, distinction between the normal and abnormal may be difficult to determine with exactness.[17] The clearly abnormal state is characterized by a great degree of thickening of the spongiosa layer with acid mucopolysaccharides[13,18,19] and by encroachment of this layer upon the other layers,[14] particularly the fibrosa (Figure 2). As the fibrosa represents the essential support of the leaflet, focal interruption of it by myxomatous infiltration causes a basic weakness of the involved leaflet. As the weakened leaflet is stretched by the pressure exerted upon it during left ventricular systole, it becomes deformed.

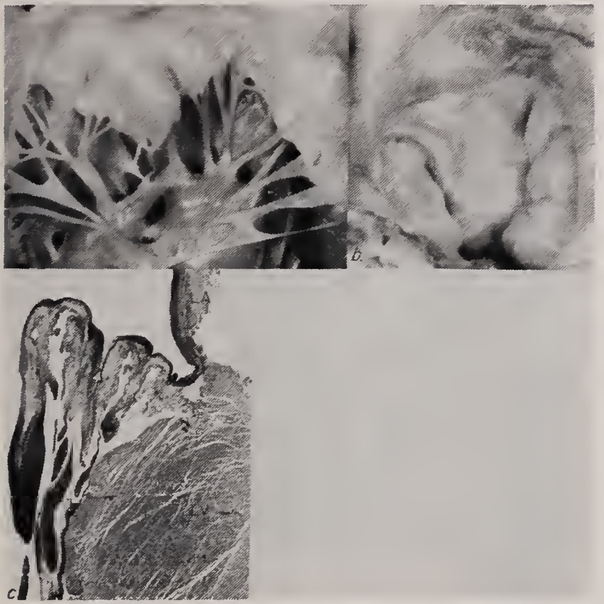

Fig. 3—Myxomatous mitral valves. (a) and (b) From a 29-year-old man with a systolic murmur who died suddenly. (c) From a 67-year-old man with subdural hematoma. (a) Characteristic interchordal hooding of the leaflets. There is variation in the thickness of the chordae. (b) The mitral valve shown in (a) viewed from above. Characteristic upturning of segments of the leaflets toward the left atrium, so-called prolapse. (c) Low power view of the left atrium (LA) and left ventricle (LV) and the posterior mitral leaflet. The hooding of the leaflet tissue occurs not only from side-to-side, as shown in (a) and (b), but also from the free edge of the leaflet toward the base, as illustrated here. The thickening of the elements of the leaflets occur between chordal insertions. The thickening of the atrial surface of the leaflet occurs predominantly at the summits of the prolapsed segments but also occurs where one prolapsed segment rubs against the other, as seen at the point of arrow. Elastic tissue stain; x 2.7.

The deformity includes an increase in the width and length of the involved leaflets and, in particular, these changes are dominant between sites of chordal insertion. This results in the characteristic interchordal hooding toward the left atrium (Figures 3(a) and(b)). The interchordal hooding is observed both from side to side and from the free edge toward the basal attachment of the leaflet (Figure 3(c)).

In the early stages, before the development of secondary changes, the leaflets are delicate and transparent and may have a gelatinous appearance. In the primary process, the chordae also participate and are classically delicate and long. The abnormally increased length of the chordae may, in part, be the result of mucinous alteration of the chordae. Though such changes have been observed, they are nevertheless uncommon, leaving the probability that the major cause of increased chordal length is a consequence of abnormal tension upon these structures by the leaflets prolapsing toward the left atrium.

The changes in the leaflets are not uniform. While both leaflets may be involved, it is usual that the process is most evident in the posterior leaflet. Even here there is variation as to the degree of involvement. Ranganathan and associates[15] found that, in the posterior leaflet, the middle third was most commonly affected with the anterolateral third of this leaflet being the second most common part to be affected. When the anterior mitral leaflet is involved, its posteromedial aspect is usually affected, while its anterolateral aspect tends to be normal. Characteristically, the commissures are not fused.

Secondary Effects

The mitral valve affected by the aforementioned primary changes may be associated with other alterations, as mentioned by Pomerance.[13] Some of these may be considered as tissue responses secondary to the abnormal hemodynamic effects of the primary disease process. Others, such as rupture of chordae, bacterial endocarditis and calcification, are considered complications.

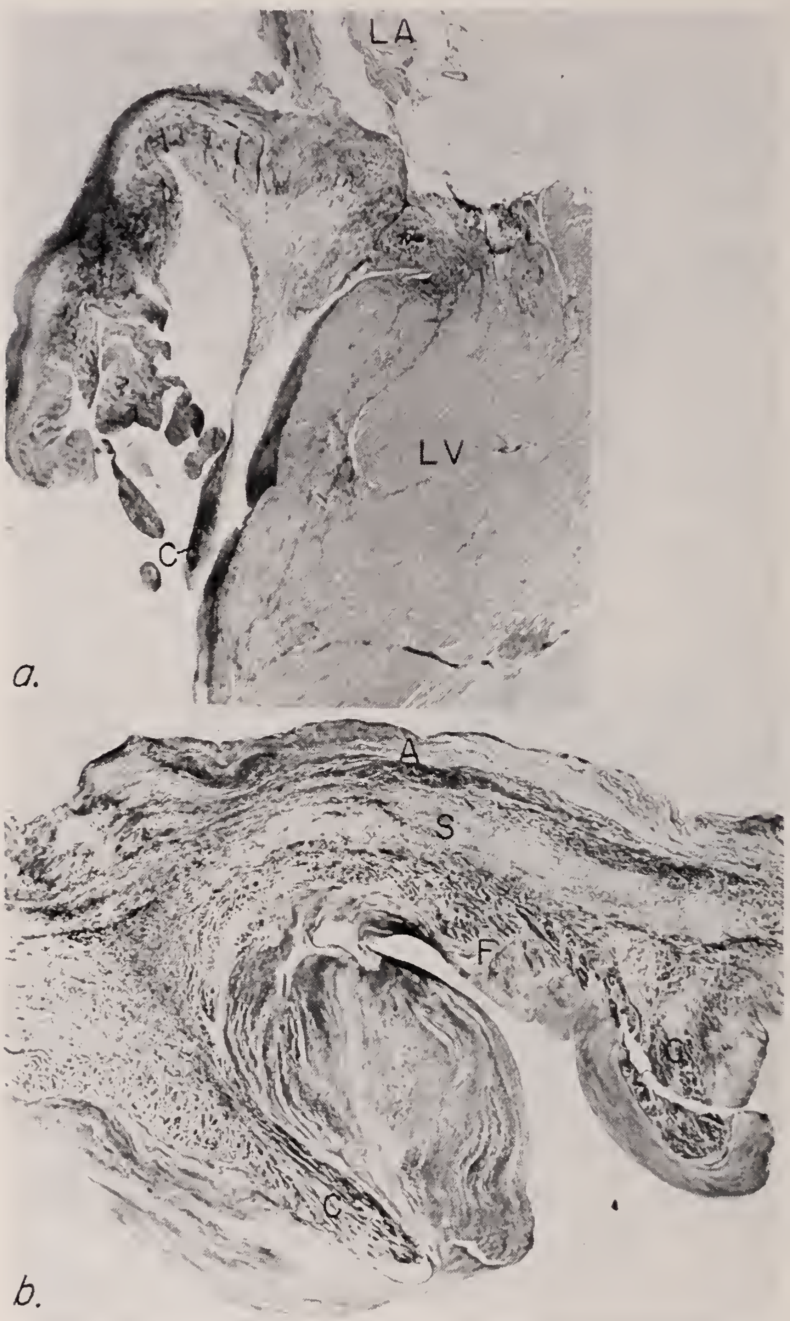

Fig. 4—Photomicrographs of myxomatous posterior mitral leaflet. (a) From a 22-year-old woman with mid-systolic click and late systolic murmur who died suddenly. The leaflet is greatly thickened, principally by myxomatous tissue. There is some fibrous reaction at the auricularis layer. A cord (C) shows thickening on its ventricular aspect and the related endocardium of the left ventricle also shows fibrous thickening. The fibrous deposits are considered secondary reactions to friction between the related cord and the left ventricular endocardium. Elastic tissue stain; x 5. (b) Posterior mitral leaflet from the case shown in Figures 3(a) and (b). Characteristic secondary changes of the myxomatous valve are illustrated. These are characterized by fibrous thickening of the auricularis (A) and pad-like thickening along the ventricular surface of the valve. Chordae (C) are involved in the reactive tissue in this zone. There is classical increase in thickness of the spongiosa (S) with encroachment upon and interruption of continuity of the fibrosa layer (F). Elastic tissue stain; x 13.

The changes secondary to the abnormal hemodynamic effects of the myxomatous mitral valve involve both the atrial and ventricular aspects of the leaflets and may also affect the chordae and the left ventricular mural endocardium.

The Valvular Leaflets

In addition to thickening of the leaflet and multiple interruption of the fibrosa by the primary process, secondary fibrotic changes occur in specific locations.

The atrial aspect of involved leaflets frequently shows thickening of the auricularis layer with collagen and elastic tissue (Figure 4). The precursor of this process may at times be observed in the form of endothelial denudation with deposits of fibrin upon the denuded surface. The changes involving the auricularis are considered secondary to abnormal friction as a prolapsed segment makes contact with its "opposite number" of the valve apparatus.

The "opposite number" for the prolapsed posterior leaflet is usually the anterior leaflet. Also, within a given leaflet one prolapsed segment may rub abnormally against another to which a fibro-elastic response also occurs (Figure 3(c)).

The changes on the ventricular aspect of the leaflet are more specific in myxomatous valves than are the changes involving the atrial aspect (Figure 4). On the ventricular aspect, connective tissue aggregates occur; these, which are composed primarily of collagen with varying degrees of elastic tissue, have a tendency to occur in prolapsing interchordal segments as connective tissue pads. The fibrous reaction on the leaflet may extend onto related chordae.[14] The interchordal fibrous pad is considered a response to the tension and stretching that occurs at the undersurface of the valvular tissue involved in prolapsing toward the atrium.

The secondary fibrotic changes may yield a gross picture wherein the pathologist, unaware of the condition, may place a label of rheumatic endocarditis upon the case. To avoid this error it is important to recognize that, in contrast to the frequent occurrence of commissural fusion in chronic rheumatic mitral disease, this does not occur in the myxomatous valve, however fibrotic it may be. Also, even when extensive fibrosis occurs, the myxomatous valve continues to show evidence of abnormal interchordal hooding. The error of calling a myxomatous mitral valve rheumatic may even be made after histologic examination. The chronically involved rheumatic valve shows complex fibrosis of the entire substance of the leaflet with loss of distinction of one layer from another (Figure 5). In contrast, in the myxomatous valve the specific layers of the leaflet are identifiable however extensive the fibrosis (Figure 6). Without the use of special stains, however, the characteristic locations of fibrous deposits of the myxomatous valve may be missed, the valve simply called fibrotic; hence, a rheumatic designation is given, the latter according to the line of thinking, "What else could it

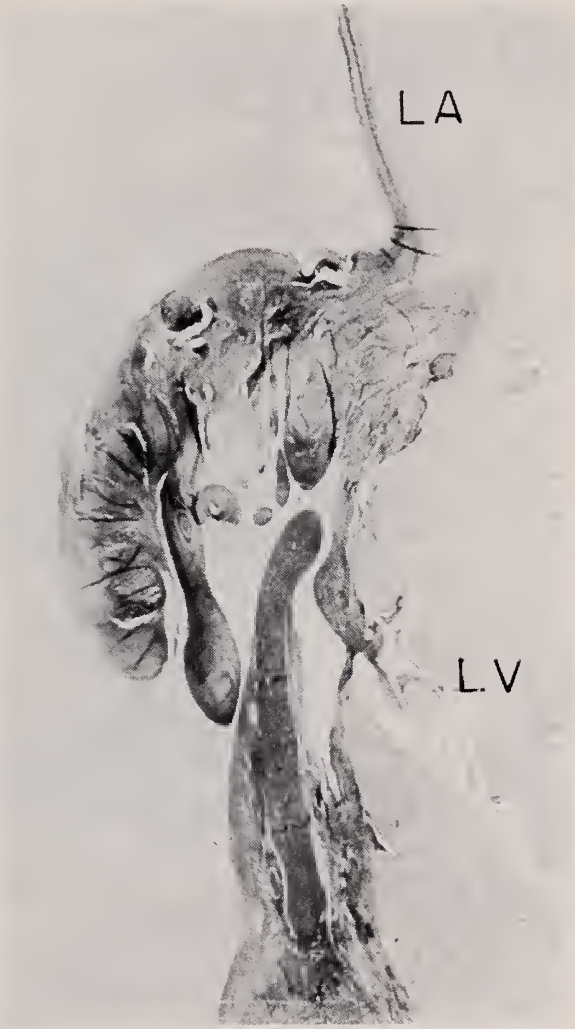

Fig. 5—Low power photomicrograph of posterior mitral leaflet and related structures in a case of rheumatic mitral stenosis. There is fibrous thickening of the leaflet with a loss in identification of the specific layers. A cord running from the papillary muscle, below, is seen to show fibrous thickening upon its surface. Elastic tissue stain; x 5.

be?" We have found stains for elastic tissue counterstained with van Gieson's connective tissue stain useful in identifying the layers and sites of secondary fibrotic changes (Figures 7(a) and (b)). Another point of caution seems appropriate. The valvular tissue that is prepared for histologic sectioning must be oriented in "true" fashion. If the tissue is oriented obliquely, the complex picture may lead to great difficulty in recognizing the specific histologic characteristic of the myxomatous valve, even with special stains (Figure 7(c)).

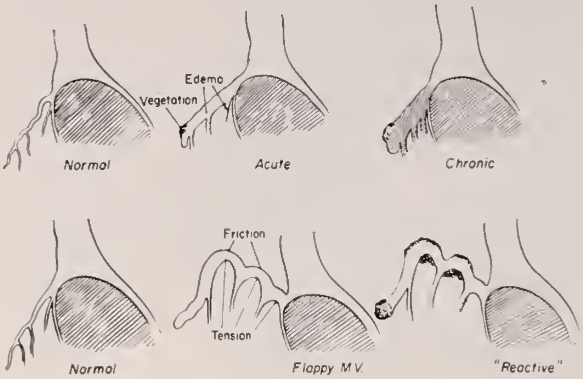

Fig. 6—Diagrammatic portrayal of the differences between rheumatic changes in the mitral valve (upper illustrations) and that in the myxomatous or floppy mitral valve (lower illustrations). The late stage (chronic) shows the loss in identification of the elements of the leaflet in rheumatic disease, while the illustration identified as "reactive" shows the characteristic secondary deposits of fibrous tissue upon the ventricular and atrial surfaces of the myxomatous or floppy mitral valve.

The Chordae

While the chordae initially are long and thin, they may become thickened by aggregation of fibrous tissue upon their surfaces.[14] As the posterior mitral leaflet protrudes to abnormal degrees into the left atrium, its chordae may come in contact with the lining of the related mural endocardium of the left ventricle. Salazar and one of us (JEE)[20] have observed that the resulting friction elicits a series of reactions upon the surfaces of the involved chordae and upon the mural endocardium. The reaction to friction upon the chordae results in deposits of fibrous tissue upon

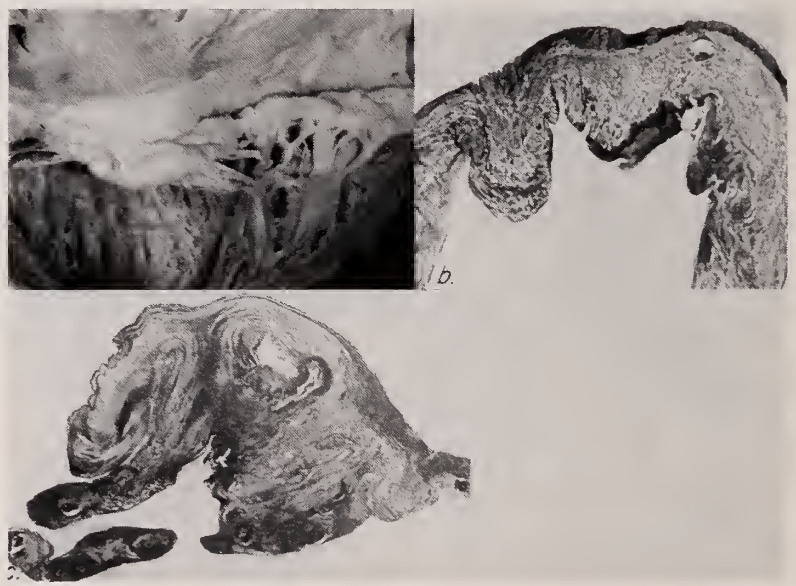

Fig. 7—Incidental finding of myxomatous mitral valve in a 76-year-old man who died of a ruptured abdominal aortic aneurysm. (a) Mitral valve and related structures. The anterior leaflet (center of illustration) shows prolapse of its posteromedial aspect, while the opposite portion of the leaflet is essentially normal. Toward the right is illustrated the major portion of the posterior leaflet which shows upturning of the leaflet and fibrous thickening of the leaflet and chordae. No commissural fusion. (b) Low power photomicrograph of posterior mitral leaflet. Characteristic changes of the myxomatous valve with encroachment upon the fibrosa by thickened spongiosa and secondary fibrous thickening both on the atrial and ventricular surfaces of the leaflet. Elastic tissue stain; x 12. (c) A semi-oblique section of the posterior mitral leaflet shows difficulty in determining the nature of the condition, in contrast to the case with which this may be identified when a true section is obtained as in (b). Elastic tissue stain; x 6.

their surfaces (Figure 4(a)). Such deposits thicken the chordae. In the left ventricular mural endocardium, the initial response to friction by chordae is represented by linear fibrous thickenings (Figure 8(a)). The thickenings may become more elaborate so as: (1) to result in coalescence of individual lesions and (2) to cause adhesion of the lower aspects of the chordae to the thickened left ventricular endocardium (Figures 8(b) and (c)). The adhesion of chordae to the mural endocardium yields a state wherein chordae that initially had been abnormally long become effectively shortened.

These ultimate responses to friction by chordae upon the left ventricular endocardium yield a complex picture that initially may be misinterpreted as the end-stage of healed bacterial endocarditis. In the book, "An Atlas of Acquired Diseases of the Heart and Great Vessels" by one of us (JEE),[21] two cases are shown* which now clearly appear to be examples of myxomatous change of the mitral valve with secondary chordal adhesion to the left ventricular wall. When initially described, however, the two cases were considered examples of healed bacterial endocarditis without history of antecedent infection.

In the myxomatous valve, the reaction to friction may cause fusion of chordae. Such changes, which are in common with rheumatic disease, give a basis for confusing the myxomatous valve with one diseased on a rheumatic basis. Distinction between these two states depends to a great extent upon the associated nature of the leaflets and of the commissures. Chordal adhesion resulting from rheumatic endocarditis causes simple fusion of chordae (Figure 9) while, in the myxomatous valve, interadherent chordae char-

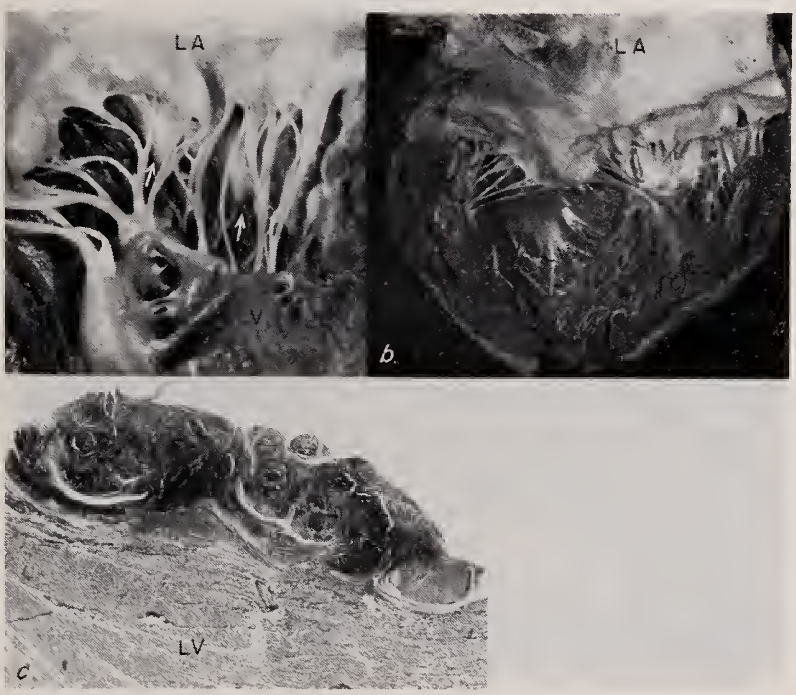

Fig. 8—Illustrations from Salazar and Edwards.[20] Friction lesions of left ventricular endocardium in myxomatous mitral valve. (a) Left atrium, the mitral valve and related left ventricle. The leaflets of the valve show prolapse toward the atrium. Beyond the chordae, many of which are thickened, the left ventricular endocardium shows linear fibrous thickening (arrow). (b) A late stage of the friction lesions that may occur upon the left ventricular endocardium in instances of myxomatous mitral valve. The endocardium of the left ventricle shows confluent fibrous thickening and incorporation into this tissue of the lower aspects of chordae. The ultimate effect is chordal shortening. (c) From the case shown in (b) a horizontal section of the left ventricular endocardium and underlying myocardium at a site of thickening of the endocardium and at which chordae have become incorporated in the endocardial thickening. Elastic tissue stain; x 6.3.

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*Pages 358-361.

acteristically are interadherent along with fusion to the left ventricular mural endocardium (Figures 8(b) and (c)).

Complications

Among the complications of myxomatous change of the mitral valve are: (1) mitral insufficiency with intact chordae, (2) sudden death, (3) rupture of mitral chordae, (4) bacterial endocarditis and (5) calcification of the posterior mitral leaflet.

Mitral Insufficiency with Intact Chordae

Non-ejection clicks occurring during the mid or late part of systole have been shown to be of mitral valvular origin[4] and are now considered a clinical characteristic of the myxomatous prolapsing mitral valve. So characteristic is this sound that it has often led to use of the term, "late systolic click syndrome" for the process of mitral prolapse secondary to myxomatous change. While this sound is commonly described in cases with myxomatous mitral valve, it should be realized that other states may elicit a similar sound. Among the other conditions are myocardial infarction with involvement of one or both papillary muscles, congenitally cleft mitral valve, and asymmetrical septal hypertrophy with subaortic stenosis.

While the click resulting from the myxomatous mitral valve may, on one hand, be associated with competence of the valve, it may, on the other, be observed in instances of mitral valvular incompetence, the latter when present being one of the complications of the myxomatous valve. When mitral incompetence is present, the associated systolic murmur has been described either as late or pan-systolic. In some cases the murmur may be associated with the characteristic click, while in others a click does not accompany the systolic murmur.[6-8] In its simplest state, the

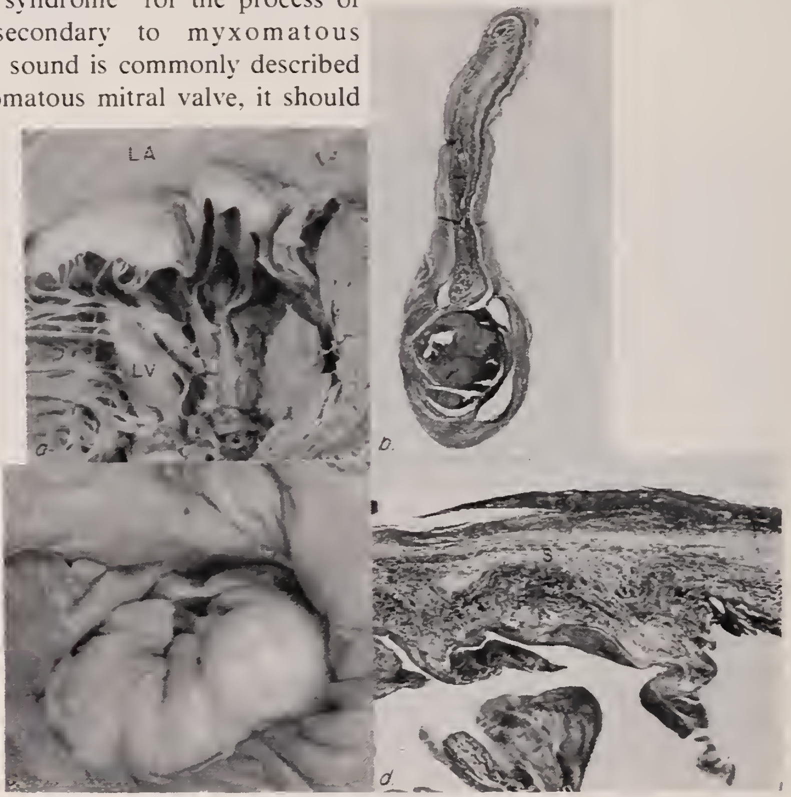

Fig. 9—From a 59-year-old man with spontaneous rupture of mitral chordae. (a) A portion of the mitral valve. The segment to which chordae have ruptured shows prolapse of greater degree than is evident in the related segments of the valve, which also show some degree of prolapse. (b) Low power photomicrograph of the ruptured end of a cord. Elastic tissue stain; x 12. (c) The unopened mitral valve viewed from above. There is widespread hooding of the leaflets toward the left atrium. (d) Photomicrograph of non-ruptured segment of the posterior mitral leaflet showing characteristic features of myxomatous change along with secondary fibrous thickening on each aspect of the leaflet comparable to that illustrated in Figures 4(b) and 7(b). Elastic tissue stain; x 13.

mitral insufficiency resulting from the myxomatous valve is associated with intact chordae. The valvular incompetence appears to result from "overshooting" of prolapsed segments beyond the opposite "number" of the valve. It is important to realize that some degree of prolapse of the mitral valve is common in the population. According to the review of O'Rourke and associates,[7] this process may be seen in as much as five to 10 percent of the population. Markiewicz and associates[22] found that, in 100 presumably normal young women, a non-ejection mitral click and/or late or mid to late systolic murmur was observed in 17 percent of the cases. In 21 of these 100 subjects, by echocardiographic study the authors found pan or late systolic prolapse of the mitral valve. These findings were statistically related to the clicks or murmurs noted.

Procacci and associates[23] studied 1169 presumably healthy young women prospectively for the presence of prolapse of the mitral valve as manifested either by a midsystolic non-ejection click or late systolic murmur and found 6.3 percent of the individuals to be afflicted. The observations of Markiewicz and associates and of Procacci and associates correlate well with the frequent observation at autopsy of incidental findings of some degree of myxomatous change of the mitral valve with interchordal hooding. Regarding the observations of the two aforementioned surveys, it remains for time to indicate the future course of affected but asymptomatic individuals. At a later date some of these may show more hemodynamic complexities.

Sudden Death

It is recognized that among patients with myxomatous change of the mitral valve sudden death is a potential complication. When histories are available such patients characteristically had shown a mid-late systolic mitral click, prolapse of the mitral valve as demonstrated by echocardiography and/or left ventriculography and ventricular premature contractions, the latter among other electrocardiographic abnormalities.

The basis for the premature ventricular contractions is not clear. Some have considered that there is ischemic change in the region of the posteromedial papillary muscle. In classical cases we have not been able to illustrate such changes. Since there is evidence of abnormal contact of chordae with the left ventricular wall, the question arises as to whether such contact may stimulate premature ventricular contraction. Another possibility suggested by Criley and associates[3] is that the prolapsing valve creates abnormal tension at the chordal-papillary muscle junctions and that this tension stimulates premature ventricular contraction.

It is important for the forensic pathologist to keep in mind the fact that sudden death may occur in this syndrome and that it has a tendency to occur in the young adult, particularly the female. Without this knowledge and by overlooking the process of myxomatous change of the mitral valve, there is the chance that the autopsy may be interpreted as revealing "no anatomic cause of death."

Rupture of Chordae Tendineae

Spontaneous rupture of mitral chordae has been considered by many to be a self contained entity. Current evidence indicates, on the contrary, that this state is a complication of myxomatous change of the mitral valve. Circumstantial evidence favoring this view is that the most common site of ruptured chordae is that involving the middle part of the posterior mitral leaflet, the same area most commonly involved in prolapse. More positive evidence comes from the fact that some patients who develop ruptured chordae have a history of having shown a mid-late systolic mitral click or late systolic murmur for some years prior to exhibiting mitral insufficiency beginning or becoming accentuated at the time of rupture of chordae.[24,25]

Most convincing evidence comes from examining valves involved with spontaneously ruptured chordae. In such valves, one finds not only prolapse of the segment of valve with ruptured chordae, but other elements of the valve, both grossly and histologically, show the same changes as in the myxomatous mitral valve without ruptured chordae (Figure 9).

Bacterial Endocarditis

A number of authors have indicated that the myxomatous mitral valve may become complicated by bacterial endocarditis.[9,26-28] Usually, the infection starts in a classical position, on the atrial surface of the valve. This may be understood as a complication of denudation of the atrial surfaces resulting from faulty contact of prolapsing segments.

A rare case has been described by Kuhn and Weber[29] in which infection started in the mural endocardium of the left ventricle at sites of friction by related chordae.

Calcification

The posterior mitral leaflet involved by myxomatous change may show focal calcification beginning at its basal aspect. In such position the calcification may be confused with calcification of the mitral ring. Current evidence suggests that the latter process has a different background from the basal calcification of the posterior mitral leaflet that, on occasion, may be a complication of the myxomatous mitral valve.

Associated Conditions

The myxomatous mitral valve is commonly associated with other conditions. In some cases, the patient shows the body physique of arachnodactyly (Marfan's syndrome). This has led to the thought that in cases without this condition the myxomatous valve is a *forme fruste* of Marfan's syndrome. Support for such a concept comes from the fact that when the mitral valve is involved, it is common that some degree of myxomatous change be observed in the other valves, and some degree of cystic medial necrosis of the aorta are commonly associated.

McKay and Yacoub[30] reported on three nonarachnodactylic patients with myxomatous mitral valve (two with ruptured chordae), in each of whom dissecting aneurysm of the aorta had begun at the site of clamping of the aorta during the operation for replacement of the mitral valve. The identified cystic medial necrosis of the aorta was considered a condition accompanying the myxomatous mitral valve.

It is of additional interest that Read and associates[9] found, among patients with "floppy" valves, certain skeletal deformities which form part of Marfan's syndrome.

Another association of interest is pulmonary emphysema. For example, among 37 cases of myxomatous valves with friction lesions of the left ventricular endocardium, Salazar and one of us (JEE)[20] observed eight cases (22 percent) with pulmonary emphysema and/or fibrosis.

In unselected material we have observed that among cases with pulmonary emphysema some degree of myxomatous valvular change is not uncommon. In these, there is a tendency for the tricuspid valve to be more obviously involved than the mitral valve. This may stem from a situation in which the valvular process in the tricuspid valve is challenged by the associated pulmonary and right ventricular hypertension.

That the connective tissue of the lung may share a defect with other connective tissue is suggested by the observation of Bolande and Tucker[31] that pulmonary emphysema is inordinately common in Marfan's syndrome.

Comment

Although some degree of myxomatous change of the mitral valve is common, this condition has received little attention until the past decade. There has, at this time, been accumulated considerable factual material concerning the clinical and related features of prolapsing mitral valve. Correlative studies relating clinical to autopsy findings indicate that, while other conditions may yield prolapse of the mitral valve and associated mid-late systolic clicks, the usual basis for this state is myxomatous change of the mitral valve.

The pathologic side to the story of the myxomatous mitral valve has lagged behind the clinical side. Reasons for this include misinterpretation of the changes as being of rheumatic origin or simply failure to identify the condition as an abnormality.

In our report we have attempted to define the characteristic gross and histologic features of the myxomatous mitral valve, features which differ both from the normal and from rheumatic changes.

The evidence indicates that the basis for ruptured mitral chordae is a background of myxomatous mitral valve, rather than being a self-contained entity.

Summary

Myxomatous change of the mitral valve is the usual basis for the mid-late systolic click syndrome, also known as floppy, billowing, ballooning or prolapsing mitral valve.

The primary process is an increase in the extent of the spongiosa layer of the leaflet with interruption of the fibrosa layer. The latter process imparts weakness to the leaflet and allows it to prolapse.

Secondary fibrotic changes occur in the leaflet, and upon the surfaces of the chordae and left ventricular mural endocardium. These changes occupy characteristic locations but have been confused with the changes of either rheumatic or healed bacterial endocarditis.

Among the complications of the myxomatous mitral valve are sudden death and "spontaneous" rupture of mitral chordae.

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Review

Coronary Vein Perfusion

The History Of

JACK KOLFF, M.D.* and W. J. KOLFF, M.D., Ph.D.*

A renewed interest in retrograde venous perfusion as a means of myocardial revascularization has prompted a review of previous attempts to use this route.

"A NEW AND EFFECTIVE mechanism for the rescue of the cardiac muscle from threatened infarction is found in the nutrition through the vessels of thebesius and the coronary veins." So wrote Dr. F. H. Pratt after his experiment on June 26, 1897.[1]

In the physiology laboratory of the Harvard Medical School he observed regular coordinated contractions intermittently for a period of an hour and a half while the coronary sinus was perfused with defibrinated arterial blood under a pressure of 12 cm of water. Pratt was trying to explain the apparent paradoxal myocardial viability and perfusion in patients who had been alive in spite of the pathological findings of severe coronary artery occlusion. In order to further explain capillary perfusion in the presence of coronary artery occlusion, Batson[2] in 1930 perfused graphite particles into dogs under conditions of increased venous pressure and decreased arterial pressure. Under those conditions graphite flakes were found in the coronary veins having become lodged there via retrograde flow through the coronary sinus. He felt that under conditions of coronary artery occlusion the pressure differential between the arteries and the veins might be reversed so that the myocardium receives its nutrition via retrograde flow into the capillaries from the veins.

It is interesting that 44 years later the pressure differential that exists in the vascular tree behind normal and blocked coronary arteries should be made use of in myocardial scanning with radioisotopes.

Cibulski[3] injected K^{43} and Kr^{85} retrograde into the coronary veins via a catheter which simultaneously occluded the coronary sinus. The radioactive material flowed preferentially into the low pressure vascular tree that exists behind an obstructed artery. Thus ischemic heart regions can be identified as radioisotopic hot spots on myocardial scans. He incidentally found that coronary arterial flow was not altered by partial occlusion of the coronary sinus when limiting the occlusion to three minutes and preventing the peak sinus pressure from rising above 30-40 mm Hg. Total coronary sinus occlusion did decrease mean aortic pressure and coronary artery inflow.

Great doubt was cast on the nutritive value of thebesian vessels by Robertson[4] in 1937. However, in experiments on dogs he ligated the coronary sinus, veins and arteries and observed that the animals survived at least several hours. Perhaps on this thread of evidence, Dr. Louis Gross[5] at the Mount Sinai Hospital in New York proceeded with studies to determine whether coronary sinus obstruction would increase intramyocardial collateral circulation. Although he was plagued by dogs dying of the "snuffles," those that survived withstood coronary sinus occlusion. Gross concluded that the pressure gradients emphasized by Wiggers[6] do indeed open collaterals and prevent or diminish infarctions and that collateral development is brought about by partial coronary sinus occlusion as well as by coronary artery constriction.

Some controversy arose after Gregg[7] could not show any benefit from coronary sinus ligation after he had ligated the coronary arteries in animals. Thornton[8] studied coronary collateral circulation and failed to find any evidence of collateral vessels 30 days after coronary sinus ligation.

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In 1941, Beck and Mako[9] repeated the experiments of Gross and found beneficial effects of coronary sinus obstruction on the mortality of dogs after occlusion of the left anterior descending coronary artery. Beck did not apply it clinically at that time; however, in later years it became one of the components of the Beck I operation[10] which consisted primarily of producing inflammation of the epicardium by asbestos and abrasion. Sprinkling inflammatory powders into the pericardial sac is still done clinically by some followers of Beck.[11]

Dr. Mercier Fauteux from Montreal, Canada, presented a manuscript in 1946 in which he reported 15 patients who had undergone coronary vein ligation between 1940 and 1946. Some had an additional pericoronary neurectomy. Most patients were symptomatically greatly improved.[12]

The first in five attempts to arterialize the coronary sinus was made by Roberts[13] in 1943. By means of a glass cannula he connected the coronary sinus with the bracheocephalic, subclavian, or inominate artery. His dogs survived for 26 hours after ligation of coronary arteries.

Beck performed his first Beck II operation on January 27, 1948.[14] A brachial artery segment was taken from the arm and bridged from the descending thoracic aorta to the coronary sinus. The coronary vein was ligated between the atrium and the anastomosis. Subsequently the operation became a two-stage procedure. First the anastomosis was made with a segment of vein and two to three weeks later the coronary sinus was subtotally occluded over a 2-3 mm probe. In 1954 Dr. Beck[15] stated that the number II operation had a 26% mortality, but anticipated that further experience would reduce the mortality. He stated that his patients were severely diseased and comparable to the medically-treated groups of patients who had a 17% mortality the first year and a 13% mortality in the second year. The operative procedure of arterializing the coronary sinus never attracted a strong following, especially after Mason Sones[16] developed his selective coronary angiography and selective indirect revascularization by the methods of Sewell[17] and Vineberg[18] became more attractive.

Although it had been repeatedly shown that arterialization of the coronary sinus decreased the acute mortality of coronary artery ligation, long term effects were in doubt. In a series of four papers between 1954 and 1956 Bakst[19-22] compared the chronic effects (six-12months) and the short term effects (one to two months) of coronary sinus arterialization. The mortality rates after circumflex coronary arterial ligation was 90% in normal dogs, 20% in the one to two month post coronary sinus arterialization group and 66% in the six and twelve month groups. Thus, Bakst was able to demonstrate a progressive decrease in the protection to the heart six and twelve months after arterialization. Retroperfusion of the myocardial capillary bed, as suggested by the low oxygen content in the backflow of divided coronary arteries, in the one to two month animals was lost in the chronic animals. The increased backflow in the six and twelve month animals associated with a high 0_2 content was evidence for the presence of intercoronary arterial anastomosis. The changes in flow can be explained by the histologic changes reported by Bakst in 1956 and Hahn and Kim in 1952.[23] They demonstrated thickening of the venous walls with intimal proliferation and eventual obliteration of the veins.

The above chronic findings did not dissuade some investigators from utilizing a coronary sinus perfusion technique on an acute basis in surgery when the aortic root had to be either cross-clamped or opened and the normal coronary arterial flow interrupted. Dr. Peter F. Salisbury[24] showed that perfusion of the coronary sinus resulted in excellent metabolic support of the left ventricle while the aorta was incised and coronary artery flow was stopped. However, since the veins of the right ventricle of dogs drain directly into that chamber, retrograde coronary sinus blood flow did not reach the right ventricle which became ischemic and eventually decompensated. Hammond[25] in 1967, inspired by Effler's 55% mortality rate for the left coronary artery reconstructive surgery, perfused the sinus and could completely occlude the left main coronary artery for a period of one hour under hypothermia at 26°C as well as normothermia at 37°C with minimal depression of the ventricular function. He used retrograde coronary sinus perfusion with an arterialized blood flow of 30-40 cc/min at a pressure of 16 mm Hg. Vascular damage occurred if perfusion pressures were greater than 16 mm Hg. Oxygen uptake was evident from consistently lower PO_2 and oxygen saturation levels in the blood obtained from the ventricles as compared to the systemic arterial blood. It is interesting that Sabiston in 1959[26] and Brown in 1972[27] show preservation of the myocardium by retrograde coronary sinus perfusion with gaseous oxygen. Sabiston was able to maintain the heart beat for up to seven hours by this method. Clinically, these techniques have been placed on a back burner and are seldom utilized.

But the pendulum keeps swinging. Today the vigorous attempts to revascularize the heart of patients with angina pectoris and the increasing number of emergency operations done for acute myocardial infarctions may on occasion turn the frustrated surgeon towards using the tempting vein. For this situation Arealis in 1973[28] recommended arterialization of the coronary vein coming from an ischemic area. Thus what Bakst and Beck learned about the beneficial effect of arterialization of the coronary sinus in preventing deaths and limiting infarct size in acute myocardial infarctions may now be utilized on a selective basis for acute myocardial infarctions. Sallam,[29] Bhayana,[30] and Olsen[31] have followed the sequence of events as they occur in an acute myocardial infarction patient experimentally by ligating a coronary artery and then observing the effects on the EKG. The myocardial discoloration, S-T changes and dyskinesia all reversed when the specific vein accompanying that ligated artery was perfused in a retrograde fashion by arterial blood. Dr. Donald Olsen[31] showed by a barium suspension injection that perfusion of the myocardium deep within the septum was possible via the veins. Whether or not this persists on a chronic basis was not proven. Gardner and Magovern[32] showed that in acute experiments oxygen was taken up by the myocardium from this new arterial blood supply and that no large A-V fistula occurred. In chronic experiments lasting up to 308 days, myocardial perfusion was demonstrated by coronary angiography and myocardial scans. They followed these chronic experiments with a clinical experience in six patients.

Arterialization of the coronary sinus has been reactivated by Moll in Poland.[33] Five patients received saphenous vein grafts from the ascending aorta directly to the coronary sinus ostium within the right atrium, after previous coronary bypass grafts had been unsuccessful. Thus, although Magovern and his group[34] have used the specific vein for extensive arterial disease and Moll has arterialized the entire venous system for patients with recurrent occlusions, we are not aware that any patient has had arterialization of the vein for acute myocardial infarction. Experimental studies suggest this is an appropriate indication.

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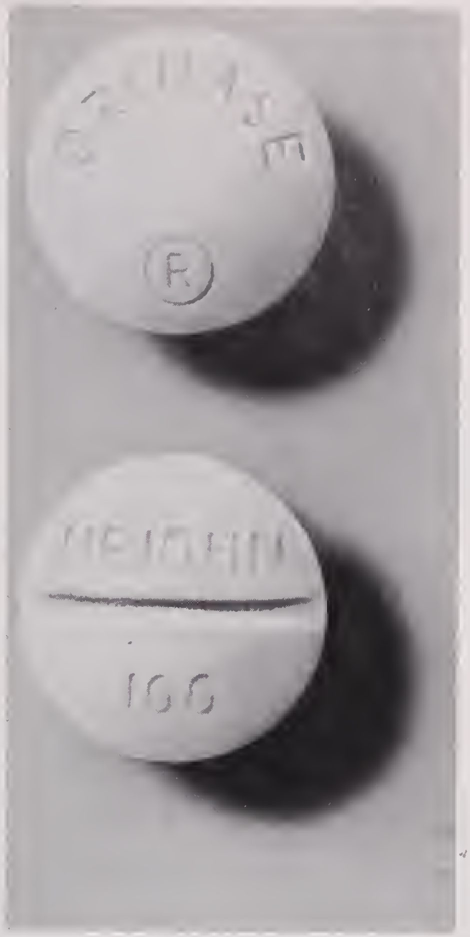
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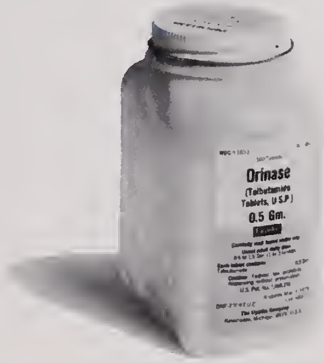
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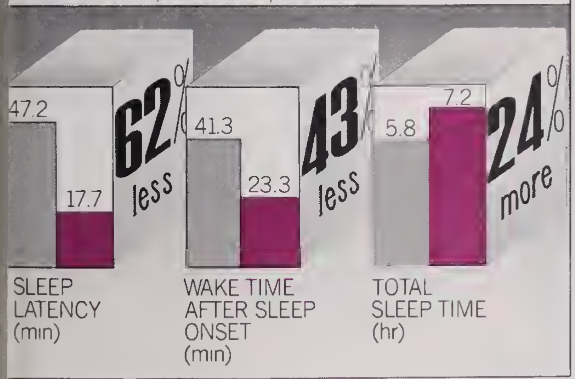
SLEEP RESEARCH LABORATORY PROOF OF EFFECTIVENESS DURING 28 NIGHTS[2]

mean % improvement in 5 patients with chronic insomnia



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Patient benefits include relative safety, infrequent morning "hang-over"

Dalmane is well tolerated, seldom causing morning drowsiness or grogginess.[4] No increase in dosage is required for continued effectiveness from night to night.[1-3] Should Dalmane be used repeatedly, periodic blood counts and liver and kidney function tests should be performed. The usual adult dose is 30 mg *h.s.*, but 15 mg may suffice for some patients and is recommended as a starting dose for the elderly and debilitated to help preclude over-sedation, dizziness or ataxia.

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- ☐ **effectiveness with a single 30-mg *h.s.* dose, maintained**
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- ☐ **less time awake during the night, maintained**

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Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum benefic effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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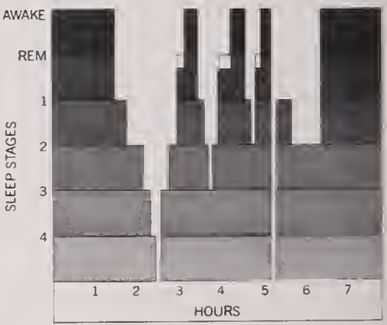

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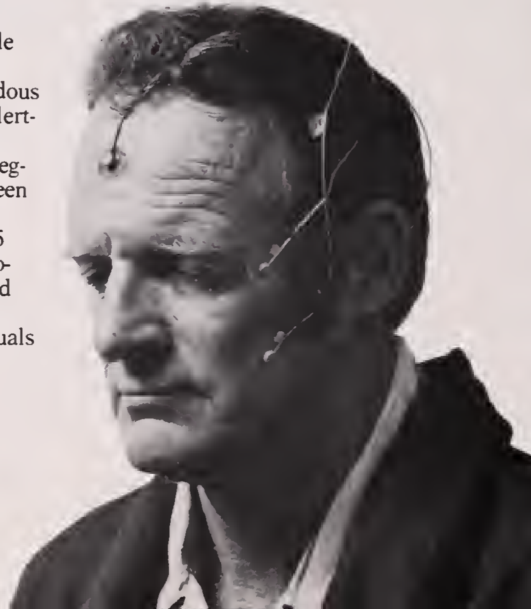

Grand Rounds

Hyperlipoproteinemias

Current Concepts

PAUL KOSS, M.D.*

Hyperlipoproteinemia is an important risk factor in coronary artery disease. Lipoproteins can be separated by various techniques. Hyperlipoproteinemia may then be classified as to type depending on the quantitative and qualitative properties demonstrated by separation. Treatment varies with the hyperlipoproteinemia type.

LIPOPROTEINS HAVE gained prominence in the last decade because of evidence that hyperlipoproteinemia is a risk factor in atherosclerosis, particularly coronary artery disease.[1-5] To discuss the etiology and treatment of hyperlipoproteinemia one must understand the structure and function of these lipid-protein molecules.[6,7]

Structure of Lipoproteins

One of the time-honored ways in which biochemists have studied biological structures is to break them down into their constitutent parts. This pattern has been followed with lipoproteins. Lipoproteins are composed of lipid and protein.

The lipid portion is made up of cholesterol, phospholipid and variable amounts of glyceride. The cholesterol in lipoproteins is predominantly esterified cholesterol.[8] The phospholipids are phosphatidyl choline and sphingomyelin. These molecules consist of both lipid soluble (hydrophobic) and polar water soluble (hydrophilic) structures and can function as "biological detergents."

Apoprotein (Apolipoprotein)

The most important component of the lipoprotein molecule is the apoprotein. It is the backbone of the lipoprotein and its metabolism probably is the determining factors in states of abnormal lipid concentration. The major methods of lipoprotein separation are two: ultracentrifugation, which emphasizes the hydrated density of the lipoprotein, and electrophoresis, which depends upon particle mobility with respect to size and charge. With these methods four major lipoprotein families have been isolated. These ultracentrifugal and electrophoretic families are respectively: High density lipoproteins (HDL) and alpha lipoprotein, low density lipoprotein (LDL) and beta lipoprotein, very low density lipoprotein (VLDL) and pre-beta lipoprotein. The chylomicron fraction, which represents dietary or exogenous glyceride and contains essentially no lipoproteins, floats on the top of the centrifuged sample and does not migrate from the origin on the electrophoresis.

Three distinct apoproteins have been described which are found predominantly in three of the four lipoprotein families described above:[9] Apoprotein A with the alpha lipoproteins (HDL); apoprotein B with the beta lipoproteins (LDL); and apoprotein C with the pre-beta lipoproteins. Because these apoproteins bind lipid tenaciously, their isolation in a lipid-free state is difficult. The best characterized apoproteins is apoprotein A, which serves as a prototype for the others.

A simplified view of the lipoproteins as presently understood is as follows: the alpha lipoprotein (HDL) fraction contains only A apoprotein, the beta lipoprotein (LDL) contains only B apoprotein, and the pre-beta lipoprotein (VLDL) contains some A, but mostly B apoprotein in combination with glyceride. Chylomicrons contain essentially no lipoprotein.

Function of the Lipoproteins: Endogenous Glyceride Transport

The primary function of lipoprotein is endogenous glyceride transport. Dietary carbohydrates, circulating free fatty acids, and glycerol are the precursors of endogenous glyceride. Once in plasma, VLDL's are quickly attacked by the same lipases that act upon chylomicrons. In a few hours, native VLDL becomes a lipoprotein intermediate shorn of much glyceride and some of its protein. Within two to six hours this lipoprotein intermediate is degraded further through the removal of more glyceride to LDL (beta lipoprotein). LDL (beta lipoprotein) is probably entirely a remnant of VLDL metabolism carrying some of the protein, cholesterol, and phospholipids originally associated with VLDL. LDL forms are then removed by the liver in two to five days.[10]

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Exogenous (dietary) glycerides are handled in a different manner independent of the lipoproteins. They are partially hydrolyzed in the intestinal lumen to di- and monoglycerides and formed into chylomicrons (0.1 microns and larger) which are released into the intestinal lymphatics. They are released into the bloodstream through the thoracic duct and the glycerides are hydrolyzed by adipose tissue, heart, liver, and other organs. Thus food intake gives rise to tidal waves of exogenous glyceride. As the delivery of dietary glucose declines, there is an increase in movement of free fatty acids out of adipose tissue. The interaction of these transport circuits of exogenous and endogenous glyceride is the basis for classifying and treating several forms of hyperlipoproteinemia.

Diagnosis, Classification, and Treatment of Hyperlipoproteinemia

Diagnosis of hyperlipoproteinemia usually involves three steps: (1) defining hyperlipidemia using cholesterol and triglyceride levels (2) conversion of hyperlipidemia to hyperlipoproteinemia; and (3) determining the etiology of the abnormal lipoprotein state. The tools available for diagnosis are clinical signs, cholesterol and triglyceride determinations, the chylomicron test electrophoresis, and ultracentrifugation. Apoprotein analysis is not yet a useful clinical tool.

Defining Hyperlipidemia

The first step, defining hyperlipidemia, requires that abnormal levels of cholesterol and triglycerides be set. Two practical rules have been suggested for this:[11]

RULE I: *Hyperlipidemia requiring diligent management exists when the values of cholesterol, triglyceride, or LDL in the Table are exceeded.*

Age (yr.)	Cholesterol (mg/dl)	Triglyceride (mg/dl)	LDL (mg/dl)
Less than 29	240	140	170
30-39	270	150	190
40-49	310	160	190
50	330	190	210

Note that these levels increase with age. These values are set high excluding only about 5% of individuals in any age group. Further hyperlipoprotein-typing is necessary for effective management.

RULE II: *Hyperlipidemia deserving some attention exists when cholesterol exceeds 220 mg/dl or TG exceeds 140 mg/dl.*

This rule should alert the clinician to possible dietary or ethanol excess.

To obtain reliable plasma samples, triglyceride value must be obtained after 12 to 14 hour fast. The cholesterol level is not significantly affected by feeding. If *baseline* values are desired, the patient must be receiving a normal diet. Wait four to eight weeks following a myocardial infarction, or similar traumatic episode. If feasible, discontinue hypolipidemic agents (e.g., estrogens, steroids, contraceptive pills, etc.) three to four weeks before the sample is to be taken.

The *chylomicron test* may be done in addition to screening cholesterol and triglyceride levels. When plasma or serum stands in a refrigerator (4° C.) overnight, any chylomicrons (exogenous glyceride) present will layer on the top. A "cream" layer means a positive chylomicron test. Chylomicrons in plasma after an overnight fast are abnormal. Generalized plasma turbidity means VLDL are abnormally increased.

Conversion of Hyperlipidemia to Hyperlipoproteinemia

The second step, which is converting the hyperlipidemia to hyperlipoproteinemia, requires more specific laboratory techniques. This usually means separation of lipoprotein families by electrophoresis. The hyperlipoproteinemias have been classified into five phenotypes on the basis of both clinical and laboratory data.[12]

Type I (Familial Lipoprotein Lipase-Deficient-Hyperchylomicronemia)

Massive chylomicronemia in the fasting state characterizes Type I. It is a rare disease (less than 50 cases reported). Inherited as a Medelian recessive, it is often expressed in infancy by eruptive xanthomas, hepatosplenomegaly, lipemia retinalis, foam cells in the bone marrow and colicky abdominal pain. In adults, episodes of pain may mimic an acute abdomen. The chylomicron test will show a thick creamy layer and clear plasma below.

This disease is due to a well-defined enzyme defect, lipoprotein lipase deficiency. Post-heparin lipolytic activity (PHLA) is decreased. The chylomicronemia is directly related to dietary or exogenous fat intake and is controlled by dietary fat restriction.

Type II (Familial Hypercholesterolemia)

Type II is a very common disease apparently inherited as a highly penetrant dominant trait. It is characterized by increased plasma LDL (Type IIa) often accompanied by moderately increased plasma VLDL (Type IIb). It is responsible for a sizable fraction of *premature* morbidity and mortality from coronary heart disease. Unfortunately, its first clinical manifestation in heterozygotes may be the occurrence of an atherosclerotic complication. Xanthomas especially over the achilles tendon, xanthelasma and arcus corneae may be detected in young adults. The presumptive metabolic defect in this disorder is the removal of beta lipoproteins. Cholesterol is 300 to 600 mg/dl in most patients with Type II; the plasma glyceride is normal in Type IIa and elevated usually to less than 400 mg/dl in Type IIb.

Type III. Broad Beta Disease, Floating Beta Lipoproteins

Type III is uncommon and characterized by an abnormal lipoprotein with beta mobility on electrophoresis; but because of increased glyceride content, it is isolated in the VLDL fraction in ultracentrifugation. The basis for this abnormal lipoprotein behavior is probably an abnormal apoprotein.[6] It is inherited as autosomal recessive. Atherosclerotic vascular disease is common with Type III. Although both coronary disease and peripheral vascular disease occur, the latter is more common in Type II than in Type III. Xanthomas of the palmar and digital creases and tuboeruptive xanthomas of the elbows are almost pathognomonic for Type III. Tendon xanthomas, tuberous xanthomas of the buttocks, xanthelasma, and arcus corneae are also commonly present. Plasma may be turbid, but is usually clear.

Type IV (Hyperprebetalipoproteinemia, Carbohydrate Induced Hyperlipemia, Endogenous Hyperlipemia

This is the most common abnormal lipoprotein pattern in the U.S. It is characterized by increased plasma VLDL of pre-beta mobility. The syndrome is undoubtedly genetically heterogenous. Relatives of patients with Types III and V often have Type IV patterns. Acute and chronic alcoholism and a host of metabolic diseases may also show Type IV patterns. Clinical signs are unusual, although arcus corneae, xanthelasma and, rarely, eruptive or tuberous xanthomas may be seen. Plasma may be clear, turbid, or frankly milky, but does not form a "cream" layer in the chylomicron test. Plasma cholesterol is usually normal or slightly elevated, plasma glycerides vary from 200 mg to 2,000 mg/dl. Glucose tolerance is abnormal and usually becomes worse with increasing age. Usually patients with coronary disease have this phenotype.

Type V. (Mixed Hyperlipidemia)

This phenotype is defined by increased plasma concentrations of both chylomicrons and pre-beta lipoprotein. It is fairly common (after Types IV and II) and, like Type IV, may be genetically heterogenous. The chylomicron test will be positive with a "cream" layer on top of turbid serum. The serum cholesterol is moderately elevated and plasma glyceride is 500 to 2,000 mg/dl. Abnormal glucose tolerance is the rule and becomes more marked with increasing age.

The above method of classification has met with wide acceptance and endorsement by WHO,[12] because of its simplicity and the availability of the laboratory techniques required. However there is difficulty in assigning a phenotype to many patients with hyperlipidemia.[13,14] While the above phenotypes are seen in pure genetic expression as "primary" hyperlipoproteinemias, they are perhaps seen more often as "secondary" to some more basic disease, or perhaps only to dietary influences. The original genetically selected group contained many patients with highly abnormal lipoprotein patterns who often had xanthomatosis. Physicians, however, often find that their patients have only mildly abnormal lipids and no physical findings to aid in diagnosis. *Frequently, the lipoprotein pattern shows increase in both beta- and* *pre-beta lipoproteins so that separation of Types IIa, IIb, and IV is difficult.* The genetic basis of Types I, IIa, and III seems to be relatively sound, but "secondary" factors, particularly diet, alcohol, and disease remain significant and often predominant contributions in patients with Types IIb, IV, and V. Some of the specific diseases which may be associated with hyperlipoproteinemia are hypothyroidism, diabetes mellitus, nephrotic syndrome, biliary obstruction, pancreatitis, dysglobulinemia, and autoimmune hyperlipoproteinemia.

Treatment

Defining the type of hyperlipidemia has proven useful in formulating an approach to treatment.[15-18] The five patterns, or Types, define the complex area of lipid transport. If the patient has a Type I pattern, there is a defect in handling dietary fat. If the Type II pattern exists, there is a defect in metabolism of beta lipoproteins. Type III, abnormal beta lipoproteins are present. In Type IV, there is an abnormality in the handling of endogenous glycerides. In Type V, there is difficulty in the assimilation of both exogenous and endogenous triglycerides. Each type of hyperlipoproteinemia responds differently to various dietary regimens and drugs.

Emergency Treatment of Hyperlipidemia

Rarely a patient will present with severe hyperlipidemia which causes abdominal pain, with or without associated fever, nausea, vomiting and leukocytosis. Immediate treatment is necessary. This situation occurs fairly often in patients with Types I and V. *Complete fasting* produces a remarkable fall in plasma lipids and disappearance of abdominal pain in 24 to 36 hours. When the patient is pain-free, a low-fat diet may be given (25% or less of calories as fat). Drugs have no part, at present, in treatment. Heparin has produced only a transitory fall in plasma glycerides and the free fatty acid rise that is produced may pose the theoretical hazard of intravascular clotting.

Long Term Management: Diet and Drug Therapy

Dietary Treatment

Proper dietary treatment is essential to successful therapy of hyperlipidemia. Drug therapy alone is often ineffective without prior or simultaneous dietary management.

1. Caloric restriction: obesity is usual in patients with endogenous and mixed hyperglyceridemia (Types IIb, III, IV, V). The VLDL or pre-beta lipoprotein increase in these diseases is derived from carbohydrate induction and increased synthesis of VLDL from free fatty acids derived from adipose tissue. Maintenance of ideal body weight is the primary therapeutic goal in these patients.

2. Calorie distribution: Decreasing the exogenous (dietary) fat intake is important in decreasing the release of chylomicrons in Types I and V. As mentioned above, decreased carbohydrate intake is important in patients with exogenous (Types IIb, III, IV, V) hyperlipidemia.

3. Fat exchange: exchange of fat rich in unsaturated fatty acids, such as corn, cottonseed, or safflower oil, for saturated fats reduces plasma cholesterol concentration and LDL cholesterol concentration (Types IIa and IIb).

Drug Therapy

In the past 20 years a great variety of drugs has been found to depress serum lipids. The therapeutically useful ones can be classified according to their effect on lipoprotein metabolism as follows:[18,24] The first group are those which *decrease lipoprotein synthesis* by (1) decreasing cholesterol synthesis, phenylbutates (clofibrate), or (2) decreasing apoprotein synthesis, nicotinic acid (B apoprotein) and androgens (A apoprotein). These drugs are most useful in decreasing VLDL (pre-beta) lipoprotein concentration (Types III, IV, V), but have been used for other types. The second group of drugs *promote apoprotein catabolism,* bile acid binding resins (cholestyramine), beta sitosterol (cytellin R), and thyroactive substances (d-thyroxine). These drugs seem most useful for Types IIa and IIb. Several field trials evaluating drug and diet therapy[19-21] are now in progress. One such study is the Coronary Drug Project.[19-20] It studied clofibrate, nicotinic acid, dextrothyroxine and estrogen in male survivors of myocardial infarction. No drug conclusively postpones deaths or recurrent myocardial infarction. The estrogen and d-thyroxine had to be discontinued because of a trend toward a greater rate of thromboembolism and death. This study only involved secondary prevention. However d-thyroxine is an effective hypocholesterolemic agent in patients without evidence of coronary artery disease. Cholestyramine, which is not being studied in the Coronary Drug Project, has been shown to be very effective for Type II patients.[22] The drug undergoing the most investigation in primary and secondary prevention is clofibrate (Atromid-S®). This drug was not only studied by the Coronary Drug Project but also by WHO in three European centers,[23] and by United Airlines Clinical Research Division.[21] Preliminary results from the latter study show a statistically significant decrease in new coronary incidents. No correlation with total mortality or cholesterol levels was seen. It was suggested that some effect other than its hypolipidemic effect may explain clofibrate's apparent effectiveness. Only extended field trials studying hyperlipoproteinemia may tell us with certainty which drug treatment is worthwhile.

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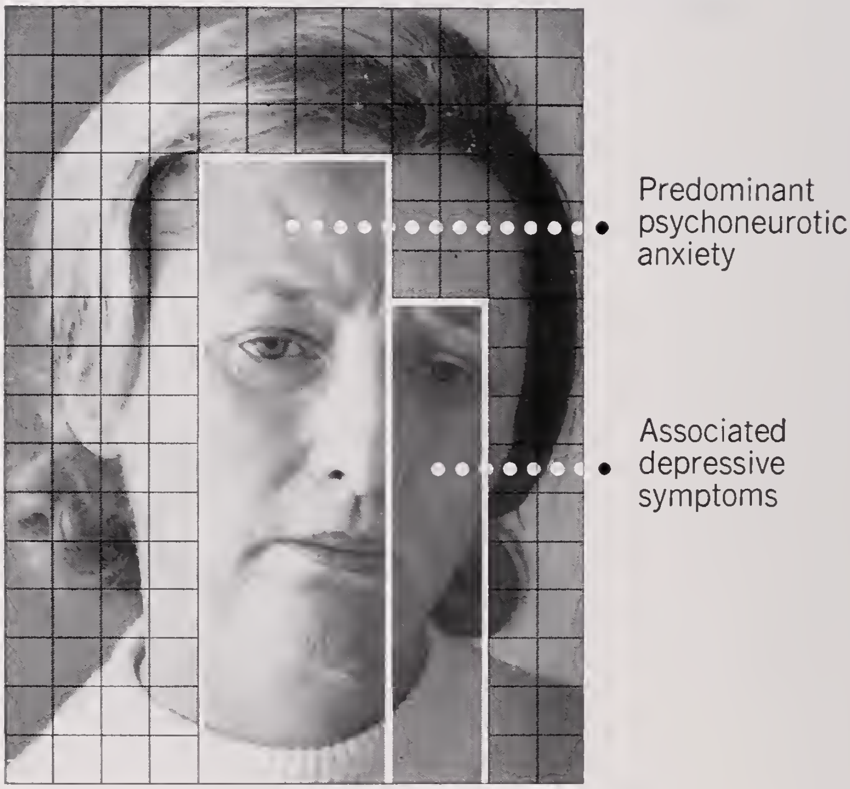
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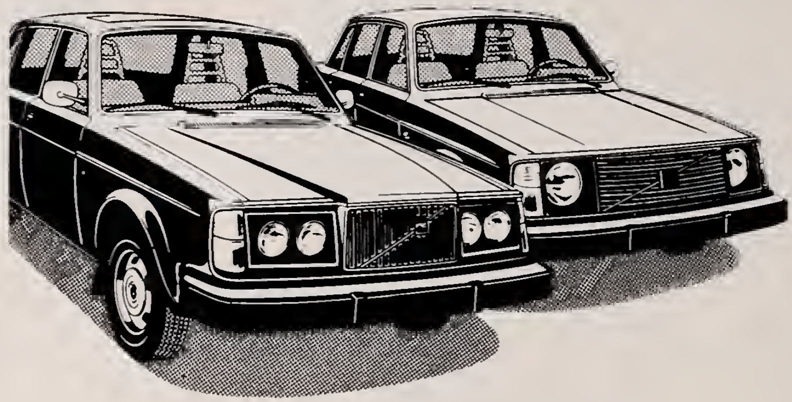

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President's Letter

Assessing Quality of Medical Care

Peer Review has been with physicians in one form or another since the beginning of medicine. In 1969, the Foundation of Health Care Evaluation was formed to make the concept more thorough, more encompassing, and more equitable. Our philosophy was to give our patients the best quality of medical care in the shortest period of time for the most reasonable cost. We began with fee review which was relatively simple but proved not to be a factor to audit to reduce health care costs. Next we began Utilization Review in a new innovation, but more equitable manner which again, at the seventy-fifth percentile was relatively easy to perform by our physicians. Utilization Review at this point in time has demonstrated that it will have the greatest impact in reducing health care costs. Admission Certification within forty-eight hours was implemented with PSRO legislation. The most difficult area of all phases of Peer Review—Quality Review—has remained in an infantile state as the debate continues over standards, criteria, and process. I have asked Dr. Donald Bell, President-Elect of the Foundation for Health Care Evaluation to discuss this problem with you this month.

RE Anonsen

Richard E. Anonsen, M.D.
President
Minnesota State Medical Association

A 76-year-old lady has been coming to the doctor's office about twelve times per year since the 1940's when she had had a carcinoma of the breast removed. A variety of thoracic and abdominal discomforts (which seemed to her succession of physicians obviously to be psychosomatic origin) aroused in her a constantly recurring concern about her cancer problem. Seemingly innumerable efforts at re-assurance and explanations of psychophysiologic mechanisms of symptoms gave only the briefest relief of her concern. Always the pains recurred in slightly different locations bringing new phone calls and visits ahead of the proposed three to four per year schedule.

Several months ago she had a myocardial infarction followed by a new pattern of exertion-related chest pains. Anticoagulation was started. A few weeks ago she bumped her head rather hard, and headaches ensued which were not a major part of her previous problems. A C.A.T. Scan was ordered, and demonstrated no evidence for subdural hematoma.

Was the ordering of this expensive test in this situation a manifestation of high quality medical care? Did it constitute an over utilization of medical facilities?

An 80-year-old lady who was still vigorous, enjoying travel and taking full interest in life developed a carcinoma of the esophagogastric junction area. A total gastrectomy was performed, and she was able to return to her previous life style for nearly a year. A few months ago dysphagia developed, and she was found on esophagoscopy to have a recurrence of the cancer at the anastomosis. Three dilatations at short intervals proved to be very difficult procedures for her to endure, but without them she could not eat and soon she would be entirely obstructed. A surgical procedure was carried out in which a funnel device was placed to allow for eating. A succession of complications followed with abscesses and external fistulae resulting in weeks of hospitalization, repeated drainage procedures, parenteral nutrient administration, and numerous drugs being used. She gradually recovered, and is looking forward to returning home for a few more weeks of life with her elderly sister, to whom her existence is of central importance.

Does this constitute high quality medical care? Is this an over utilization of medical facilities?

Who Can Write Regulations?

What individual, committee, or agency can possibly hope to establish guidelines or regulations that can realistically deal with the endless variation of disease processes in the combinations that occur in people who have the limitless variety of personal and social situations that confront physicians every day of their careers. How can anyone give sharp definitions of which decisions constitute high quality decisions, and which ones do not. Regulations demand sharp definitions.

Liberal Philosophy

For those people who dream, plan, and labor to achieve the "great society," the availability of high quality medical care for every member of society is an axiom as basic as any to be found in mathematics. Nothing could be more fundamental in the liberal political philosophy than the idea that optimum medical care be delivered to everybody. Mr. Aneurin Bevan, leader of the labor party in England in the late 1940's, typified belief in this social philosophy with his prediction that the delivery of total and free health care to the British people would so improve the health of the people that absenteeism would diminish, productivity increase, and the cost of health care would go down as disease retreated before the advances of medical science and its applications to the health problems of the people.

Mystique of Health Care

The failure of achievement of any of these laudible goals has not deterred people of liberal political persuation from pursuing the goal of optimum medical care for all members of society. It is, of course, impossible (and even inappropriate) to disagree with the stated objective of excellent health care for all people. It is worth noting, however, that other public services commonly speak of *minimum* standards (minimum nutritional requirements, minimum housing standards, etc.) rather than optimum services. No one advocates filet mignon or six bedroom houses for all of society. Perhaps the reason for this difference lies in the mystique of health care as opposed to the practicalities of supplying other basic human needs.

PSROs

In 1972 stimulated by these philosophic principles, Senator Bennett of Utah attached an amendment to a piece of tax legislation calling for the Secretary of HEW to establish a system of organizations that would supervise the administration of high quality medical care to the people of this country. Labeled Professional Standard Review Organizations, these organizations thus assumed legal responsibility for the supervision of the delivery of high quality medical care as the result of a law based on this philosophic principle without there having been a clear definition of just what "high quality medical care" is.

The government, which is accustomed to issuing myriads of regulations pertaining to virtually all of our behavior and activities in specific terms which are easily regulated, (your house must be 35 feet from the road, a loan company cannot ask the marital status of a loan applicant, etc, etc, etc,) issued regulations to the effect that "high quality care is to be delivered, the PSROs are to assess it and assure its quality."

Thus those groups which have been attempting to act as PSROs have had the double burden of both supervising a service and also trying to define that which they are supervising. The enormity of the task coupled with the legitimate and understandable divergence of opinions has meant delay after delay in the establishment of operational quality of care assessment procedures much to the frustration of those who have given many dozens of hours to the task.

How Does One Enforce a Philosophy?

How does one proceed to realistically assess *that which actually is a philosophical ideal?*

No service is as complex as medical care and its ramification. Any attempt by nonmedical people to define high quality of medical care is almost certain to be hopelessly simplistic, and thus either unenforceable or catastrophic to actual medical care in its attempted enforcement.

For example, I recently heard a consumer advocate attempt to define high quality medical care as "making the correct diagnosis and making the people well." Despite the fact that doctors themselves cannot always agree on what constitutes high quality medical care, we must push on with the job of its definition and the attendant assessment because we are now under the force of law to do so.

As a practical fact, in this situation, high quality medical care can be identified as the absence of poor care. To take this matter out of the abstract, we must concentrate in identification of poor patterns of care. Thus to a great extent, the quality of medical care consists of the appropriateness of the physician's reaction to the illness and abnormalities of health of a patient. This in turn can be divided into two general areas.

First, it is the appropriate application of medical science and its attendant technology to the illnesses and abnormalities of the health of people (to be strongly emphasized is the word appropriate). Secondly, there is the concept that illness is always surrounded by factors of personality, emotion, and social situation which constitute much of the challenge and burden of those that seek to administer medical care to the individual. High quality medical care must allow for these factors.

Considering the second element first, it should be apparent to all concerned that this aspect of medical care is entirely beyond evaluation and regulation. The key to high quality care in this consideration is flexibility; the flexibility that allows a patient to easily change doctors if the current one does not have the personal qualities of interest or kindliness desired; the flexibility that allows a doctor and patient together to decide on a course of treatment unfettered by third party regulators; the flexibility that allows the physician to individualize treatment of a complex personality-illness-social problem that a given patient presents to him without regulations attempting to dictate to him that which he must do or not do in any given situation.

Use of Audits

Concerning the assessment of the application of medical technology to a patient's illness, there is a disagreement as to how this can be accomplished. The technique of such assessment lies in the use of audits, but what does one audit? There has developed a disagreement between those who would audit the outcome of medical care and those who would audit the process by which it is delivered. This debate has consumed countless hours of committee meetings and the failure to reach agreement on this question has a lot to do with the sterility of efforts to develop "operational" audits so far. Perhaps a constructive compromise can be reached that would assist doctors in getting over this hurdle of the outcome-process impass.

Use of Outcomes

The concept that outcome of medical care is all that really counts is appealing to many. This concept would be totally valid if we had great ability to accurately and in reasonable time assess the results of the application of technology to health problems. Those who hold strongly to this viewpoint seem to ignore the fact that these conditions do not prevail in much of medical care. They also ignore the fact that wide variations in quality and quantity of care can be (and are being) tolerated under the guise that outcome seems to justify these questionable practices. One specific example; daily injections of 1,000 mcg. of Vitamin B-12 to all hospitalized patients regardless of diagnosis is justified by the "outcome" that these people "felt better" as a result of this therapy. The true validity of medical care is based on a combination of rationale (it makes sense to try to bring increased circulation to ischemic myocardium either medically or surgically), and carefully controlled studies of the results of the techniques applied to these problems. Such studies are the responsibility of those who conduct research and publish their results in the medical literature. This type of outcome evaluation is far beyond the ability of hospital committees to assess. Thus the "outcome" advocates must recognize the practical limitations of the hospital audit in assessing the quality of medical care delivered to the community.

Place for Physician Judgment

The advocates of "process" audits are frequently accused of promoting "cookbook" medicine, and certainly this fear has some validity especially if poor judgment is used in the construction and administration of the audit. The fear that guidelines will become regulations has considerable support in the manner in which the government agencies have intruded into the affairs of virtually all businesses and enterprises with countless regulations. Yet it seems that we in medicine have so far for the most part been able to run our own ship. We still have the opportunity to establish realistic guidelines to help assure the delivery of quality health care within the PSRO system. To recognize the hazard of auditing the process of health care does not necessarily justify the abandonment of this approach to auditing however. To argue that many doctors would "order the book" for a given type of clinical problem, is to abandon the argument that we in medicine must be allowed to use our own judgment in dealing with these problems. If that were to be our response to a process audit, then we indeed do need regulation from those outside the medical profession. A good process audit should simply serve to study the appropriateness of the response of the physician or hospital staff to a clinical problem.

Practice Habits

I would combine the elements of this definition of high quality of medical care into the concept that it is embodied in the *practice habits* of the physician as he or she encounters diverse problems. These habits should be subject to appraisal through well designed audits containing appropriate and realistic outcome objectives and process items.

A recent study conducted in Tennessee pertaining to the use of Chloromycetin involving a large number of physicians is a good illustration of the potential value of this type of evaluation. It showed that a small number of physicians habitually wrote a large number of prescriptions for this drug for inappropriate reasons. Their practice habits in this regard were not commensurate with high quality medical care.

Conclusion

To conclude, it seems that there is truth in both camps, and that quality assessment can and should be established containing both outcome factors (where these can be reasonably ascertained), and process factors carefully drawn. These audits should be constructed to search for poor practice habits which can realistically be changed by education if possible and individual regulation if necessary.

The health care foundation's concept of local autonomy in each hospital, supervised and coordinated by the foundation which is entirely local in its membership is ideally suited to accomplish this task.

Donald C. Bell, M.D.
President-Elect
Foundation of Health Care Evaluation

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Editor's Notebook

Health Care 1976: Part III

Medical Leadership and Social Responsibility

There is an obvious cure for Failure—and that is Success. But what is the cure for Success?—Daniel J. Boorstin, Democracy and Its Discontents, Random House, 1974.

In this series, this is the third and last editorial I shall write about the United States Health System. As you may know from reading my first two pieces, I base these editorials on what I picked up at a six week course on Health Systems Management at the Harvard Business School.

Harvard is not to blame for what I say here. I have carefully filtered facts and ideas gathered there through my own prejudices before expressing them.

Our Problem

After listening and talking to university professors, public health officials, hospital administrators, government planners, and others engaged in managing organizations in the health field, I conclude we doctors have a problem: a successful product. Americans now take for granted good health and the technology that helps to create that health. Good health care has become "a right," as perhaps it should be. In any event Americans are demanding more and better care and expecting dramatic results.

Our Contribution

These exaggerated expectations are the price of our success. But exaggerated expectations are hard to pay for. The government has contributed to these expectations through generous programs. We have also contributed by leading people to believe ultimate answers to good health lie in curative Medicine rather than in good health habits.

Questions

I kept asking myself questions as I went through the course. How can we, as practicing physicians, persuade the American public that Medicine doesn't cure all ills? At the same time, how can physicians control cost, improve health, and widen access? And how do we maintain a leadership position in helping to determine America's health policies?

I have no easy answers.

But I think we start by recognizing a few realities.

Many Voices

First, we are no longer the principal party making health policy decisions. Instead we are one of many. These include consumers, labor union leaders, corporation executives, government officials and activists of all genre. We are not even the only voice in Medicine, as we once were. In 1900, physicians made up two of every three people in the health field. Today one of twelve people in the Health Care Industry is a physician. Many of these nonphysicians are highly trained professionals who have an important say in decision making.

Big Business

Second, Health Care is big business, the second biggest industry in the United States after automobiles. It employs four million people, consumes about $130 billion dollars, and by 1980 will take more than 10 percent of the Gross National Product. Health Care is, in short, too big to be ignored.

Society of Organizations

Three, America has become a society of institutions. Most Americans work directly or indirectly for large organizations. Sooner or later, we physicians are going to be subjected to the disciplines of organizational behavior. What we want done will require organizational leverage to do. As Peter Drucker, one of the fathers of modern management and a social critic, puts it: "Our society has become, within an incredibly short fifty years, a society of institutions. It has become a pluralistic society in which every major social task has been **entrusted** to large organizations—from producing economic goods and services to health care, from social security and welfare to education, from the search for new knowledge to the protection of the natural environment."[1]

Social Responsibility

Four, in the last ten years, a new and significant concept, "social responsibility," has arisen. This concept holds that major institutions—hospitals, medical schools, universities, churches, corporations—are "responsible" for anticipating social problems and issues, for easing or solving them, and even for setting social goals. In part, this concept represents a disillusionment with government. Great Society programs, including Regional Medical Programs, have taught us a government who tries to do too many things for too many people without specific purposes or specific skills not only fails to do anything but fails to satisfy anybody. So society has turned to organizations to get specific tasks done.

Physicians

Once we recognize these realities, I believe we can do something to help shape changes occurring in the Health System. I am reasonably optimistic about the future for physicians. For one thing, society still holds physicians in high esteem. A poll in the August 22 edition of the *New York Times* gives these percentages for Americans who rated "honesty and ethical standards" of various American occupations as "high" or "very high":

Medical doctors	55%
Engineers	48%
College Teachers	44%
Journalists	33%
Lawyers	25%
Building Contractors	22%
Business Executives	19%
Senators	19%
Congressmen	14%
Labor Union Leaders	13%
Advertising Executives	11%

I am particularly optimistic about the prospects for physicians in Minnesota, for I think this state's physicians have a gift for anticipating social demands and for organizing to meet those demands.

So what can we physicians do to meet our "social responsibilities"?

Meeting Our Social Responsibilities

1. We can acknowledge uncontrollable costs, poor health habits, and difficult access to good care are fundamental problems. We can also take concrete steps to correct these problems by a) trying to keep people out of hospitals and shortening their stay there as much as possible; b) directly in-

forming the American people that the road to improved health lies through good health habits, rather than through more technology and more money poured into the system; and c) making people more aware, through such mechanisms as the Hennepin County Directory for Physicians and through encouraging young physicians to become family physicians and to form rural groups, that we are making our services more accessible.

2. We can be aware that our true opportunities are serving those outside the profession, rather than protecting those inside. Somehow we must project the image (and back that image with concrete action) to Americans that our goal is service to them, rather than to ourselves. This is partly why the Minnesota Medical Association organized its Division of Socio-Economic Affairs—to convince legislators, consumers, and the press, that we are serving the public as best we can. What we need to do now is persuade the public, through the media and through our own actions, that we are taking positive steps to control costs, improve health, and widen access.
3. We can take more time evaluating expensive new technology. This evaluation should include studies of alternatives, randomized clinical trials, and cost benefit considerations. These studies will require that we educate ourselves in the disciplines of statistics and decision analysis.
4. We can become more management minded. Management is not "administration;" it is leadership. It is organizing the strengths of people to get the right things done in a systematic and purposeful way. In the future I think we should encourage (and pay for) physicians to learn more about the fundamentals of organizational leadership.
5. We can recognize the virtues of a pluralistic society, with its different organizations as one of the strengths of America. A pluralistic health system, with a mix of private and public services, of individual and group practices, is probably the soundest approach in this diverse country. The better health systems in the world outside the United States are not "unitary" systems, such as in England, but "mixed" systems, such as in Germany, Canada, or Australia.
6. We can learn techniques of industrialization so that we can handle more patients more effectively, efficiently, and economically.[2] These techniques include a systems approach to human services, division of labor, concentration of specialty talents, economies of scale, and a production-line, yet personalized, processing of patients. Mayo Clinic, for example, has mastered many of these techniques and has shown this can bring efficiency, excellence, order, and speed to the service process. Other examples of successful institutions are automated medical laboratories, prepaid health groups, and ambulatory surgical centers. I am not advocating the industrialization of medicine, but in selected situations, I think the techniques of industrialization may help us serve and satisfy more patients.

Conclusion

What is the cure for our success? The cure is working and thinking through our problems, building on our strengths, focusing on opportunities to serve the people, training ourselves in organizational matters, building organizations to get the right things done, and leading those organizations.

Richard L Reece MD

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Contents—October, 1976

Volume 59:10
Pages 663-734

COVER PHOTO—"St. Anthony Falls" 683

PRESIDENT'S LETTER—Assessing Quality of Medical Care

Richard E. Anonsen, M.D., President, Minnesota State Medical Association
Donald C. Bell, M.D.,
President-Elect
Foundation of Health Care Evaluation 667

EDITOR'S NOTEBOOK—Health Care 1976—Part III

Medical Leadership and Social Responsibility
Richard L. Reece, M.D., Editor-in-Chief 671

ORIGINAL CONTRIBUTIONS

Microsurgery for Cerebellopontine Angle Tumors
Donald L. Erickson, M.D. 677

Transcutaneous Electrical Stimulation for Chronic Pain Relief
Henry H. Stonnington, M.D., B.S., F.R.C.P. et al. 681

Reticulum Cell Sarcoma of Brain in a Patient with Chronic Lymphocytic Leukemia
Marvin Napgezek, M.D. 684

Neurologic Urinary Bladder Dysfunction
Gaylan L. Rockswold, M.D. et al. 687

EDITORIALS

Reduction Mammoplasty
Lyle V. Kragh, M.D. 699

LETTER TO THE EDITOR—Minnesota Clean Indoor Air Act
C. Richard Guiton, M.D. 701

SPECIAL ARTICLE—Reduction Mammoplasty
Carl O. Rice, M.D. 707

TRAUMA—Fractures and Dislocations of the Spine
David S. Bradford, M.D. and Roby C. Thompson, M.D. 711

GERONTOLOGY—Medical Care for an Aging Population
Winston R. Miller, M.D. 727

MSMA HIGHLIGHTS—The Mystery of Medicaid 693

MINNESOTA STATE BOARD OF MEDICAL EXAMINERS—
Notices of Suspension 726

CONTINUING MEDICAL EDUCATION 691, 704, 710, 733

BOOK REPORTS 721

CLASSIFIED ADVERTISEMENTS 722

INDEX TO ADVERTISERS 734

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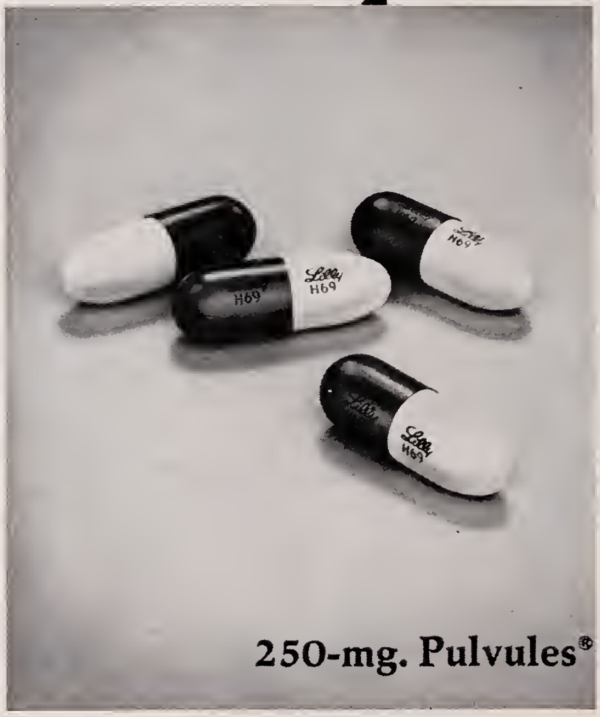

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Microsurgery for Cerebellopontine Angle Tumors

DONALD L. ERICKSON, M.D.[*]

The benign cerebellopontine angle (C.P. angle) tumor, because of its slow growth, can achieve a large size, indenting the brain stem and intimately insinuating itself amongst the cranial nerves, before it becomes clinically evident. For that reason, surgical excision is difficult and potentially hazardous. The operating microscope has helped reduce the morbidity and mortality associated with the removal of these large tumors. Early diagnosis, while the tumor is small, would greatly enhance the care of these patients.

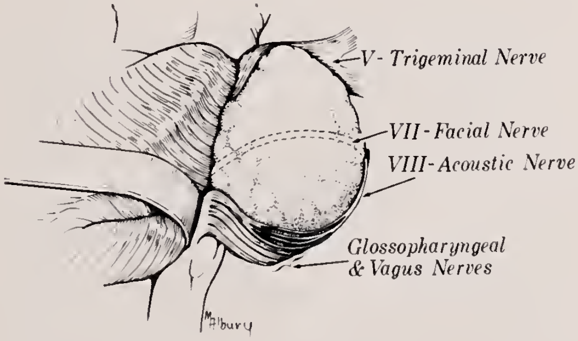
THE INSIDIOUS ONSET and growth of C.P. angle tumors makes early detection difficult, and therefore the surgeon is often presented with a large tumor indenting the brain stem and stretching the surrounding cranial nerves. One then faces the challenge of totally excising a benign lesion while avoiding the morbidity and mortality which will result if adjacent nervous tissue is damaged. The operating microscope provides the excellent lighting and magnification necessary for this technically difficult surgery.

The operating microscope has been used actively by the otolaryngologists for the past two decades. Its value for removal of acoustic tumors was demonstrated by House, and has now become a standard operating room instrument for this procedure.[6,7] This article will discuss the diagnosis and surgery of cerebellopontine angle tumors with special reference to preservation of the seventh nerve. Clinical results and surgical technique will be reviewed in the fifteen patients who underwent this surgery, by the author, during the past two and one-half years. A patho-anatomic explanation of the mechanisms which produce the clinical features of this tumor will be discussed.

Patho-Anatomy[*]

Growth Pattern

Acoustic neurinomas are the most common C.P. angle tumors, and the remaining discussion will relate to that specific lesion. Thirteen of the tumors in this series were acoustic neurinomas, one was a fifth nerve neurinoma and another a venous hemangioma. The acoustic tumor most often arises from a vestibular branch of the eighth nerve, in or near the internal auditory meatus. As it enlarges, the eighth nerve is progressively destroyed, while the seventh nerve is stretched around the capsule of the tumor. The first symptomatology is related to the eighth nerve in the form of tinnitus or hearing loss. Initial hearing loss is most typically related to speech discrimination, and may appear in a subtle fashion in such



Figure—Acoustic tumor in situ.

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[*] Refer to Figure.

things as use of the telephone. Although the seventh nerve also exists through the internal auditory meatus, and is therefore anatomically involved quite early, clinical dysfunction is rarely seen until the tumor is several centimeters in diameter. As the tumor enlarges, it begins to indent the adjacent brain stem and the fifth cranial nerve becomes stretched over its anterior superior pole. The patient may then experience mild ataxia or incoordination of the extremities and corneal sensation will be diminished. With further enlargement one is likely to find reflex asymmetry, more marked cerebellar findings and hypalgesia of the face, as well as of the cornea. Obstruction of spinal fluid circulation around the brain stem may be impaired, producing hydrocephalus and increased intracranial pressure.

Growth Rate

One must remember that this is often a slow growing tumor, and may have a clinically quiescent period of several years between the initial symptoms of auditory acuity disturbance and the subsequent findings of brain stem and fifth nerve dysfunction. The author has seen two cases where six years elapsed between the first evaluation of acoustic tumor and the subsequent presentation of a large C.P., angle mass. In both of these cases a tumor was suspected early, but the techniques then available were inadequate to detect small tumors. Large tumors present an increased operative risk because of the distorted neural structures, but also in part, because arteries supplying critical brain stem function may be adherent to the tumor capsule. Damage to these small vessels may produce a disabling brain stem infarct or even rapid death.[1]

Diagnosis

Clinical Examination

Because the patients most typically complain of symptoms related to auditory function, the otolaryngologist is usually first to initiate diagnostic tests for acoustic tumor. There are a number of specialized audiological tests which can increase one's suspicion of the presence of an eighth nerve tumor, or conversely establish an entirely different diagnosis.[8,9] There is, however, a large indeterminant group of patients in which a firm diagnosis cannot be established, and more specific diagnostic tests must be instituted.

Neurological examination is of no help in diagnosing small tumors and spinal fluid examination will likely be normal. In the older literature, elevated CSF protein was consistent, but we now know it is often normal in patients with small tumors.[7]

Radiological Examination

Neuroradiology provides our only certain means of diagnosis. Polytomograms of the internal auditory meatus may show enlargement of the affected side.[12] Computerized axial tomography is also a significant adjunct, but with the present state of technology, tumors less than one centimeter in diameter will not likely be demonstrated. With future improvements, this technique may well provide the ideal screening test. The clivogram (posterior fossa myelogram), which is an extension of spinal myelography, is undoubtedly the most precise test. In skilled hands the radiologist can position the dye in a normal internal auditory meatus, definitely demonstrating the absence of a neoplasm, or into the abnormal side where a neoplasm of several millimeters in diameter will stand out against this contrast background.[5]

One is therefore faced with the dilemma of deciding which patients with early hearing loss should be subjected to this diagnostic procedure. I would again emphasize the long silent period between the first symptoms of acoustic tumor, and the time when it becomes clinically obvious. The obvious tumors are sufficiently large to present potential serious complications during their removal, and it is therefore extremely valuable to diagnose these tumors at an early stage. One must accept that a number of patients will be subjected to an unnecessary clivogram if one hopes to find C.P. angle tumors early in their development. In skilled hands the clivogram has very little morbidity, compared with the potential disaster of an overlooked tumor. It might therefore be prudent to perform clivography on patients with unilateral hearing loss in which the otolaryngologist cannot establish a definite etiology.

Surgical Technique

Basic Approaches

There are basically three surgical approaches to the cerebellopontine angle tumor. One is a translabyrinthine approach, in which the otolaryngologist, using magnification, enters the lateral mastoid area and identifies the seventh nerve by cautiously removing surrounding bone with a high speed drill. He then follows this nerve back into the internal auditory meatus where the tumor is encountered and removed without major exposure of the posterior fossa.[6] This is suitable for small tumors, but because of the limited exposure, is unsafe for large tumors where the brain stem is involved. It has the additional disadvantage of destroying the labyrinthine structures, and therefore eliminating any possibility of preserving residual auditory function. A second otolaryngological approach is through the middle fossa, transpetrous, wherein the internal auditory meatus can be reached without destroying the labyrinthine structures. This again is suitable for very small tumors, but is an extremely specialized operative technique with even more limited exposure. The most common approach to the cerebellopontine angle tumor is via a sub-occipital craniotomy, which was the procedure used in this series. This has the advantages of providing adequate exposure for removal of large tumors and preserving the labryrinth in hopes of retaining auditory function in small tumors.[10]

Suboccipital Approach

A laterally placed suboccipital craniotomy gives ready access to the tumor with minimal cerebellar retraction, and only once in this series was it necessary to resect cerebellar tissue for tumor exposure. A high speed drill is then used to remove the posterior portion of the internal auditory meatus, which exposes the most lateral extent of the neoplasm. The tumor is then removed by internal decompression and gradual separation of the capsule from surrounding brain stem, fifth, seventh, and lower cranial nerves. The seventh nerve can be identified either where it arises from the brain stem medially, or where it exists, lateral to the tumor through the internal auditory meatus. The fifth nerve is almost invariably easy to separate from the tumor capsule, but the seventh nerve may be extremely thin and adherent, requiring sharp dissection to separate it without damage. Any traction applied to the thin, delicate nerve at this stage may disrupt it. Any arteries adherent to the tumor which supply the brain stem must be preserved at this stage if one is to avoid serious morbidity or mortality. The inferior anterior cerebellar artery, in particular, may loop laterally along the tumor and then swing medially to supply medulla and pons.[1] All of these aforementioned procedures are significantly enhanced by the magnification and lighting system of the operating microscope.

Results

Tumor Size

None of the acoustic tumors in this series were classified as small, that is, less than one centimeter in diameter. Two tumors fell into the giant group, where the anterior inferior aspect of the tumor had reached the clivus, and all the cranial nerves from six through eleven were stretched around its capsule. The remaining eleven tumors were intermediate to large tumors, being three or four centimeters in diameter.

Morbidity

There were no mortalities in this series. One patient had persistent elevation of CSF pressure, producing a pseudo meningocele, which required wound revision. She developed bacterial meningitis, which responded well to antibiotic therapy, and she has subsequently made an excellent recovery.

Seventh Nerve Function

The seventh nerve was preserved anatomically in all but one patient. Seven patients had what appeared clinically to be complete seventh nerve dysfunction following surgery, in spite of anatomical preservation of the nerve. To date, six of these patients have had progressive recovery of seventh nerve function in the months following surgery and we anticipate recovery in the other one as well. Facial nerve recovery in three of these patients occurred within two to three months, but in the patients with larger tumors, some nine months elapsed before any clinical or electrical signs of recovery were evident. Other cranial nerves, such as the twelveth or eleventh, can be anastomosed to the extracranial seventh nerve to restore tone to facial muscles, but the cosmetic result is often less than ideal. It is important therefore, when one is convinced that the seventh nerve is anatomically intact, to allow sufficient recovery time before subjecting the patient to an anastomosis procedure.

Discussion

History

The development of C.P. angle surgery is in itself an interesting story. Six internationally known neurosurgeons reported series of acoustic tumor removal, prior to 1915, with mortalities ranging from 68 to 86%.[11] Harvey Cushing then reported a series in 1917 with a mortality of only 11%.[2] Most of his, however, were incomplete removals, a situation which would not be generally acceptable today. Walter Dandy, Cushing's pupil, reported in 1941 some 46 cases of complete tumor removal with only a 10% mortality.[3] All five of his operative deaths were in patients who were in coma prior to surgery, and if one discounts those patients, his mortality was zero. It is of interest to note, that Dandy preserved the seventh nerve in only one of these 46 patients, and stated that, "paralysis of the facial nerve must usually be accepted as a necessary sequel of the operation." His technical accomplishment, however, cannot be underestimated, and is emphasized by comparing it to a series presented by Olivercrona in 1949, where there was a 25% mortality in 304 cases.[4] Many of these were incomplete removals, and still, in only 30% of the cases was the seventh nerve preserved. McCarty reported a recent series of 132 patients from Mayo Clinic with a 5% mortality and 52% preservation of the seventh nerve.[10]

Clinical Presentation

This fascinating, but uncommon tumor, represents only 5-10 percent of intracranial tumors.[12] As already indicated, the surgical removal of a small tumor is technically much simpler, and presents less risk to the patient. The long silent clinical period between the first audiological symptoms and the clinically detectable brain stem and fifth nerve symptoms, may represent a number of years and a dramatic increase in tumor size. A high index of suspicion is therefore necessary if one is to diagnose these tumors at an early stage. Clivography, at this time, is the definitive test for small tumors.

Treatment

The advent of the operating microscope has enhanced our ability to deal successfully with these neoplasms. The excellent lighting and variable magnification allow preservation of critical arteries and less critical, but important, adjacent cranial nerves. With these technical advantages, one can even hope to improve on Dandy's results.

Although the final chapter on acoustic nerve tumors has not been written, the story has improved remarkably over the past fifty years. With the combined efforts of family physicians, otolaryngologists, neurologists, neuroradiologists, and neurosurgeons, the outlook for future patients should be much brighter.

Summary

The operating microscope is an invaluable instrument in the removal of cerebellopontine angle tumors. This procedure should now have a small mortality and morbidity. Disfiguring seventh nerve palsy should be an uncommon sequelae to the surgical excision of these lesions. As newer diagnostic techniques become available and physicians become more aggressive in early diagnosis of hearing loss, we expect that tumors will be found when they are small, allowing not only preservation of the seventh, but also of the eighth cranial nerve in a certain number of cases.[10]

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Transcutaneous Electrical Stimulation for Chronic Pain Relief

A Pilot Study

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A series of 182 patients with chronic, unrelieved pain underwent transcutaneous electrical stimulation in a department of physical medicine and rehabilitation. Of the 182 patients, 81 (45%) got initial relief and elected to procure an electrical stimulator for home use. Of these 81 patients, 48 (59%) initially obtained complete relief, but after three months, only five (6%) still had complete relief. This experience indicates that transcutaneous electrical stimulation gives some benefit, although the effect may be a placebo one or of short duration.

FOR THOUSANDS OF years, it has been known that counterirritation can relieve pain.[1] Gammon and Starr[2] showed that deep pain could be reduced by the non-noxious application of electrical, thermal, or tactile stimuli. They postulated that suppression of pain occurs within the central nervous system. The use of electricity as a counterirritant antedates written records. The early residents of the Mediterranean region applied shocks from the electrical ray of torpedo fish.[3] For at least 50 years, departments of physical therapy have used interrupted static, galvanic, and sinusoidal electricity.[4-6]

Since Melzack and Wall[7] introduced their theory of gate control in 1965, there have been several reports indicating that transcutaneous electrical stimulation (TES) is useful in controlling pain.[8-10] The goals of the present pilot study were to determine whether: (1) pain can be relieved by TES, (2) relief can be maintained, (3) some areas of pain are more susceptible to relief than others, and (4) some types of pain are more easily relieved than others.

Materials and Methods

All patients were referred to the Department of Physical Medicine and Rehabilitation, and all fulfilled the following criteria. The patient had to have a full diagnostic workup to exclude the need for any medical, surgical, or physiatric treatment. Treatment had to have failed previously, the pain had to be chronic, and the patient had to be willing to be treated as an outpatient.

One type of transcutaneous stimulator was used: the Stimulation Technology EPC Personal Stimulator. The pulse generated is a modified rectangular pulse, and the output has a constant characteristic, which is adjustable from 0 to 50 mA. The duration of the pulse is adjustable from 50 to 500 μs, and the frequency is adjustable from 15 to 180 pulses per second. Surface electrodes, each made of medical graded stainless steel in a cellulose sponge, were used for contact with the skin, and tap water was used as an electrolyte.

The electrical stimulator was applied to three sites: the central area of the pain, the area over a related nerve trunk, and the area over an unrelated nerve trunk. The selected related nerve trunk was the trunk that innervated the center of pain, and if this was not easily accessible, the nerve trunk from the same spinal segment that supplied the center of pain was selected. The

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selected unrelated nerve trunk was always on the side of the body opposite the center of pain, and if the center of pain was in a lower extremity, a nerve trunk in an upper extremity was selected, or if the center of pain was in an upper extremity, a nerve trunk in a lower extremity was selected. The responses were graded as complete pain relief, partial pain relief, no pain relief, and pain aggravated. More precision in grading by using percentage of pain relief was considered, but such precision could not be reliably obtained. Because of this, the category of partial pain relief probably contains a wide range of unreliable responses.

Each patient was seen by a physiatrist, who prescribed the method that was to be used for each patient and carried out by physical therapists. The physical therapists were trained in all aspects of this modality. A prescription for the three variables on the electrical stimulator (output, pulse width, and rate) was given. However, either the therapist or the patient could change these variables if necessary. The usual prescription was an electrical output that did not give pain or muscle contraction but did give a sensation strong enough to be felt by the patient. The pulse width usually was 100 μs, and the rate was usually about 100 impulses per second. The application of the stimulator was continued until the patient, therapist, and physiatrist were satisfied that either no relief was obtained or there was partial or complete relief. Each patient had at least two sessions per day, and each was allowed to borrow the electrical stimulator overnight after receiving the proper instructions on its use.

The patient was then asked to decide whether he wanted to rent or buy the stimulator. If he either rented or bought the device he was classed as a "buyer," but if he chose neither, he was classed as a "nonbuyer." Every patient was followed up by means of a questionnaire after an average period of three and a half months, with a range of two to six months. The pain was categorized into six groups: post-traumatic, postsurgical, neuropathy and neuroma, chronic low-back pain, chronic neck pain, and others. The patient's medication was never altered and psychologic advice was not given.

Results

A total of 182 patients (77 males and 105 females) fulfilled the criteria for inclusion in the study. Of the 182 patients, 81 (45%) obtained initial relief and procured the stimulator (buyer group); of these, 48 (59%) got complete relief. Of the 101 nonbuyers, 15 (15%) obtained relief from the stimulator. Some of the 15 claimed complete and lasting relief and therefore believed that they had no further need for the stimulator. However, most of this group reported that they could not afford to buy the stimulator or that they had to await the decision of an insurance company regarding the purchase. Thus, of the 182 patients in the series, 96 (53%) obtained initial relief.

The buyer and nonbuyer groups were essentially similar. The mean age of the 81 buyers was 50.9 years, with a range of 23 to 98 years, whereas the mean age of the 101 nonbuyers was 52.3 years, with a range of 14 to 89 years. Of the 81 patients in the buyer group, 38 (47%) were males and 43 (53%) were females, whereas the nonbuyer group consisted of 39 (39%) males and 62 (61%) females.

Comparisons of the six different diagnostic subgroups between the buyer and nonbuyer groups revealed no essential differences (Table 1).

The application of the electrical stimulator over the area of pain gave relief (either complete or partial) to most patients (Table 2). Many pa-

TABLE 1
Pain Relief and Transcutaneous Electrical Stimulation

	Stimulator			
	Buyers (81 patients)		Nonbuyers (101 patients)	
Category	No.	%	No.	%
Post-traumatic	10	12	11	11
Postsurgical	11	14	2	2
Neuropathy and neuroma	12	15	14	14
Chronic low-back pain	32	40	47	46
Chronic neck pain	6	7	7	7
Others	10	12	20	20
Total	81	100	101	100

TABLE 2
Initial Pain Relief Obtained by 81 Stimulator Buyers and Site of Stimulator Application*

	Relief			
	Complete		Partial	
Site	No.	%	No.	%
Central area of pain	30	37	36	44
Nerve trunk	18	22	20	25
Related	13	16	16	20
Unrelated	5	6	4	5
Ttoal	48	59	56	69

*Some patients had relief at more than one site.

tients had relief of pain from stimulation at more than one site. Most patients, however, had a preference for one site.

Follow-up revealed that, although 48 (59%) of the stimulator buyers initially obtained complete relief, only five (6%) had complete relief at three months (Table 3). A total of 18 patients (23%), including three (4%) whose pain was aggravated by the modality, had no relief at follow-up. This decrease in the percentage who obtained relief applied equally to all the diagnostic categories.

TABLE 3
Pain Relief at Follow-up of 81 Stimulator Buyers

	Original treatment		Follow-up (3 mo)	
Result	No.	%	No.	%
Complete relief	48	59	5	6
Partial relief	33	41	58	71
No relief	0	0	15	19
Pain aggravated	0	0	3	4
Total	81	100	81	100

Of the 15 nonbuyers who initially claimed variable relief (partial to complete), eight maintained their improvement (two complete) for at least three months. Of the 86 who had no initial relief, 13 indicated in the questionnaire that they had some relief at three-month follow-up. None of these had complete relief at three months, and none had used any other form of therapy other than that received at our clinic.

Discussion

The immediate results of electrical stimulation in our pilot study are similar to those noted in other series.[8,10] However, the results at follow-up are much different. Forty-eight (59%) of the buyer group who originally were relieved had complete relief initially. After three months, only 6% (five patients) had complete relief. Thus, of the total 182 patients, only seven patients (five buyers, two nonbuyers) still claimed complete relief after three months. It is true that there were still approximately 72% of the buyers whose pain was partially relieved at three months. We found the group that obtained partial relief difficult to assess.

These findings may indicate that the original responses were placebo effects only or short-lived at best. Despite the failure of persistence of good response by those who used the electrical stimulator, the stimulator still would be of as much value as other counterirritants,[2] such as heat or cold. Interestingly, stimulation of the area of pain itself gave the best results, thus reinforcing the theory of counterirritation. We believe that the electrical stimulator is a modality to be used in a department of physical medicine and rehabilitation. The results indicate that further study (controlled trial) of the procedure is indicated.

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Cover Photographs
"St. Anthony Falls"

The top cover painting is St. Anthony Falls as it appeared in 1848 and is a photograph of the painting by Henry Lewis which hangs in the Minneapolis Institute of Arts, (Courtesy of the Minneapolis Institute of Arts).

The bottom photograph is a region of St. Anthony Falls as it appears in 1976 snapped by Dr. Farrell Stiegler, the Cover Editor of MINNESOTA MEDICINE,

Reticulum Cell Sarcoma of Brain in a Patient with Chronic Lymphocytic Leukemia

MARVIN NAPGEZEK, M.D.*

An 81-year-old woman receiving chlorambucil for chronic lymphocytic leukemia was found at autopsy to have a reticulum cell sarcoma involving only the brain. Although the incidence of this type of brain tumor is known to be increased in renal transplantation patients on immunosuppressives, this is, to my knowledge, the first time it has been found in association with chronic lymphocytic leukemia. Since reticulum cell sarcoma of brain is relatively radiosensitive, it is of particular importance to clarify its relationship to diseases in which long-term immunosuppression is carried out.

PRIMARY RETICULUM cell sarcoma of brain is an uncommon lesion, originating from the reticuloendothelial cells of the Virchow-Robin spaces.[1] It accounted for only 40 of 8070 intracranial tumors reported from the Armed Forces Institute of Pathology,[2] for a frequency of 0.5%, and was found in only 23 of 25,200 autopsies performed at the Massachusetts General Hospital from 1940-1970, or slightly less frequently than once per 1,000 autopsies at that institution.[3]

Although lymphocytic leukemia with co-existent reticulum cell sarcoma has been previously reported,[4] the case reported here is believed to represent the first in which primary reticulum cell sarcoma of brain has been found in the presence of lymphocytic leukemia.

Case Report

An 81-year-old widowed white female was admitted to Northwestern Hospital October 7, 1974 for evaluation of asymptomatic bilateral carotid artery bruits. Chronic lymphocytic leukemia had been diagnosed in 1966 when her peripheral blood, drawn during a routine office visit, showed a leukocyte count of 18,800/mm^3 with 88% lymphocytes. She was followed without therapy until October, 1968 when the leukocyte count was 49,900 with 90% lymphocytes, and treatment with chlorambucil was begun. Within six weeks the leukocyte count had fallen to 7,700 with 73% lymphocytes. Chlorambucil 2 mg P.O. twice weekly was continued from November, 1968 through July, 1974. On bimonthly office visits, the spleen was intermittently palpable but the nodes remained non-palpable.

At admission she was a pleasant, spry lady appearing younger than her stated 81 years. Her blood pressure was 140/75, pulse 82 and regular and temperature 97.0 orally. Neurologic examination was not remarkable. There was no adenopathy and liver and spleen were not palpable. Bilateral carotid bruits were heard.

Laboratory findings included hemoglobin 12.9 grams %, a leukocyte count of 8,600 with 53% lymphocytes and a serum protein electrophoresis that was normal except for albumin of 3.37 grams % (normal 3.4-4.4). Carotid angiograms showed bilateral intracranial fibromuscular hyperplasia but no midline shift of intracranial vessels and no tumor vessels.

On October 10, the patient was discharged without surgery, and was mentally alert. One week following discharge, she was noted by family members to be forgetful, and neglectful of personal appearance, and she was transferred to a nursing home.

On November 21, 1974 the patient was admitted to Northwestern Hospital with a two-week history of progressive lethargy. She was obtunded on admission,

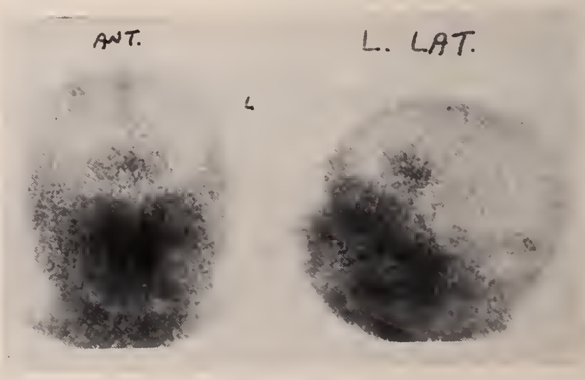

Fig. 1—Brain scan showing location of the tumor.

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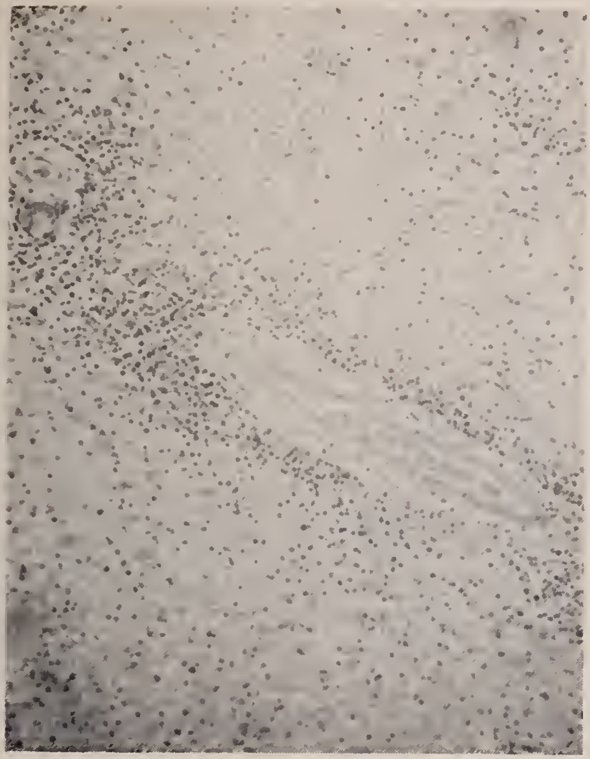

Fig. 2—Low-power view of the tumor showing typical perivascular cuffing by tumor cells (magnification 10x).

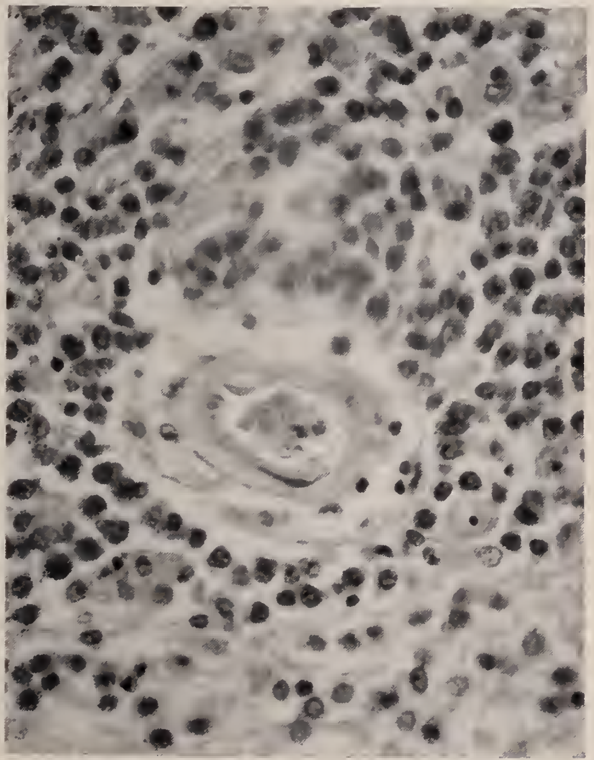

Fig. 3—Higher power view of tumor cells (magnification 45x).

responsive only to deep pain. A brain scan revealed a single deep-seated lesion in the area of the anterior corpus callosum (Figure 1). The patient remained obtunded and died on December 1, 1974.

Autopsy revealed an 8 x 5 x 5 cm area of softening and hemorrhage in midline of the fronto-parietal area, extending into the corpus callosum. Microscopic examination of this area revealed reticulum cell sarcoma with characteristic perivascular cuffing* (Figures 2 and 3). The bone marrow showed a small focus of lymphocytic infiltration. No other organs showed tumor involvement.

Discussion

Reticulum cell sarcoma of brain has previously been reported in the presence of a compromised immune system. It has occurred in patients with Wiskott-Aldrich syndrome[5] and with immunoglobulin A deficiency.[6] Both patients had cellular and humoral immune defects. It has also occurred in a patient with paraproteinemia in whom the adequacy of cellular immunity was not discussed.[7]

Convincing evidence has been accumulated indicating that renal transplant patients are at increased risk to develop reticulum cell sarcoma of brain. Schneck and Penn[8] found brain tumors in 11 of 184 transplanted patients, nine of which were reticulum-cell sarcomas. In reviewing the records of 6297 individuals reported to a kidney-transplant registry, Hoover and Fraumeni found the risk of reticulum-cell sarcoma for this group to be 350 times greater than expected.[9] No specific immunosuppressive agent could be implicated.

Although the possibility exists that in our patient reticulum cell sarcoma arose in a site of pre-existing leukemia, this is unlikely since chronic lymphocytic leukemia rarely undergoes blastic change,[4] and lymphocyte transformation by phytohemagglutinin in this disease is markedly impaired.[10,11]

In chronic lymphocytic leukemia, a disease in which the immune deficiency is impaired gamma globulin synthesis,[12,13] it is believed that the chance of developing a second primary tumor is not increased.[14,15] However in the reports cited,[14,15] there is no specific mention of type or duration of chemotherapy. Perhaps the patient with chronic lymphocytic leukemia whose cellular immunity is under long-term suppression by anti-leukemic agents is indeed at increased risk of developing a reticulum cell sarcoma of the brain. Since these tumors are relatively radio sensitive,[1,3 7] further understanding of the relationship between chronic lymphocytic leukemia and reticulum cell sarcoma of brain could be of practical significance to patients with leukemia.

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*Tissue sections kindly reviewed by Dr. J. H. Sung, University of Minnesota Neuropathology Laboratory.

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UPCOMING: 1976 Fall House of Delegates

When? November 19 & 20, 1976

Where? Registry Hotel, Minneapolis

Neurologic Urinary Bladder Dysfunction

Evaluation and Treatment at the University of Minnesota

GAYLAN L. ROCKSWOLD, M.D., Ph.D.*; WILLIAM E. BRADLEY, M.D.†
GERALD W. TIMM, PhD. (EE)‡ and SHELLEY N. CHOU, M.D., Ph.D.#

Urinary bladder dysfunction remains one of the most debilitating and frustrating complications of neurologic disease. The resultant urinary incontinence and malfunction is not only a psychological and social nuisance, but the chronic effects on renal function and general health are often very serious. The purpose of this article is to describe the various methods used at the University of Minnesota Neuro-Urological Laboratory to test neurologic bladder dysfunction. From the results which can be obtained we will attempt to outline an approach to treatment. Our experience was based on the evaluation of over 600 patients with neurogenic dysfunction of the urinary bladder. Patient's diagnoses included multiple sclerosis, diabetes mellitus, Parkinson's disease, spinal cord injury, congenital malformations of the spinal cord, cerebrovascular disease, spinal cord and brain tumors and nocturnal enuresis of childhood.

THE NEUROLOGIC HISTORY and examination remain very important in diagnosing the primary neurologic disease and the site of the lesion. In relation to the voiding disorder an attempt was made to distinguish between supraspinal dysfunction of the micturition reflex and segmental deficits in bladder and sphincter innervation.

Patients with supraspinal neurologic involvement frequently complained of frequency and urgency and were unable to contract the anal sphincter on command. The sphincter, however, revealed good tone. Patients with involvement of the sacral spinal cord or cauda equina most frequently had difficulty initiating voiding and emptying the bladder. A lax anal sphincter and perianal numbness were occasionally present.

The general neurologic evaluation, however, was of limited value in specifically delineating the nature of the bladder dysfunction and in the selection of the proper therapeutic approach. Also, patients with neurological disease had unrelated bladder difficulties such as obstructive uropathy or stress incontinence. On the other hand, patients with a normal neurological exam had bladder symptoms as a consequence of disease of the nervous system.

Neuro-Urological Examination

It would be ideal to be able to distinguish between neurogenic and non-neurogenic bladder disease with a single diagnostic test. Despite the fact cystometry was introduced nearly 100 years ago, this was still not possible. In most instances, however, by employing the series of tests listed below we have been able to determine neurologic from non-neurologic causes of bladder dysfunction.

Cystometry

The basic neuro-urologic diagnostic procedure was cystometry. This consists of retrograde filling of the urinary bladder through an indwelling catheter with either gas or liquid with constant recording of intravesical pressure. We have preferred carbon dioxide over saline because of much faster filling times and less artifact related to the decreased viscosity of air.[3] There was no more than a 10% decrease in volumes recorded due to the compressibility of CO_2 compared to saline at the intravesical pressures recorded.[8]

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The principle observation made from the cystometrogram was the presence or absence of a detrusor reflex. The reflex stimulus was passive distension of the bladder, and the response was a strong contraction of the detrusor muscle producing an intravesical pressure rise. If a detrusor reflex was evoked, the patient was asked to suppress the reflex as a test of detrusor reflex volitional control. Inability to suppress the reflex is an event frequently termed an uninhibited detrusor reflex (Figure 1). Since this often occurs with a low volume reflex threshold it has been termed detrusor hyperreflexia. Clinically, these cystometrogram findings were associated with the sensation of urgency and frequent percipitate voiding with little voluntary control.

In the case of complete absence of a detrusor reflex on cystometry, the patient usually had difficulty in initiating effective voiding and in emptying the bladder.

Anal and Urethral Sphincter Electromyography

The anal sphincter electrical activity was studied with the aid of an anal plug with externally mounted recording electrodes.[4] A bipolar concentric recording electrode was mounted on a urethral catheter in order to study urethral sphincter activity. This electrode design obviates the discomfort and inconvenience of the insertion and reinsertion of needle electrodes. The total electrical output of the sphincter was measured in contrast to the localized sample recorded by needle electrodes. Patients were asked to contract volitionally the sphincters to determine if supraspinal innervation was intact. Our studies confirmed that the external anal and external urethral sphincters contract and relax synchronously.[1]

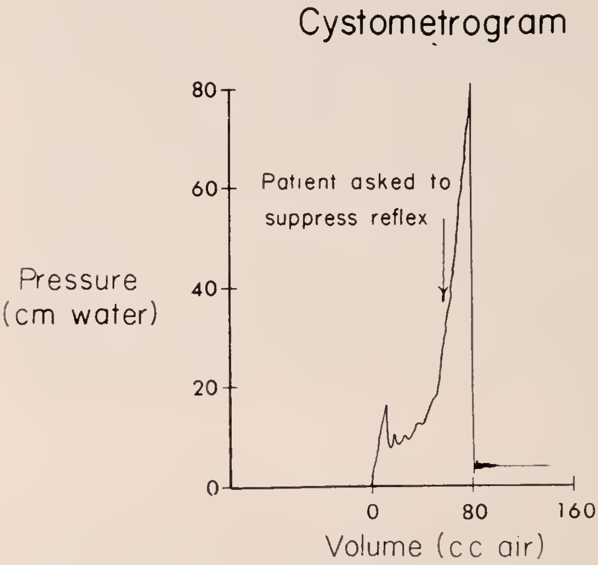

Fig. 1—Cystometrogram demonstrating detrusor hyperreflexia.

Electromyography of Voiding

Cystometry and electromyography of the sphincters were done simultaneously in order to study the interaction of the two essential elements of voiding, detrusor contraction and sphincter function. This was termed electromyography of voiding. Normally there was reduction in the level of sphincter EMG activity with bladder distension and cessation with a detrusor contraction. This attenuation of sphincter activity could be voluntarily reversed in the normal patient. Patients with sphincter dysfunction had difficulty with this task.

Electromyelography

This is a new technique which is still in the developmental stages.[2,13] By stimulating the nerve endings in the mucosa of the urethra and bladder a contractile response can be recorded in either the external anal sphincter or external urinary sphincter (Figure 2). The presumed pathway when stimulating the bladder wall is via the pelvic nerves and cauda equina to the sacral spinal cord. The pudendal nerve nucleus is activated resulting in contraction of the sphinc-

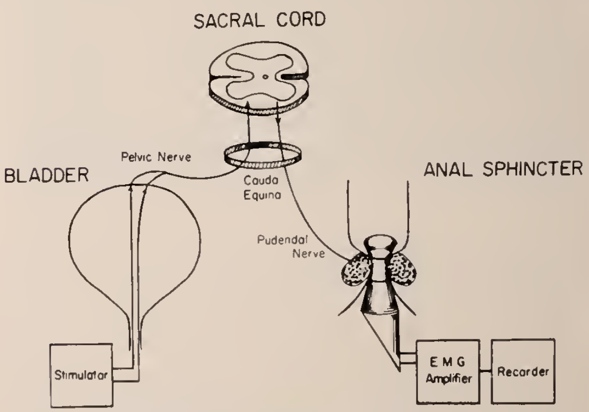

Fig. 2—Diagram of technique and neural pathways involved in electromyelography.

ters.[5] The latency in normal patients has been determined to be 60-80 msec. Subarachnoid spinal anesthesia obliterates the response refuting the possibility that it could be due to local stimulus spread.

This appears to be a useful clinical tool to determine the anatomical integrity of pathways from the bladder and urethra to the sacral spinal cord including the pelvic nerves, cauda equina, conus medullaris, as well as the pudendal nerves. Various lesions have been shown to produce either increased latencies and depressed responses or complete loss of response depending on the extent of the lesion.

Urinary Flow Rates

The measurement of urinary flow rates was a good measure of the effectiveness of detrusor contraction and sphincter relaxation.[7] When coupled with intravesical pressure measurements it can aid in defining anatomic obstruction of the urethra.

In addition to the special neuro-urological tests described above routine studies of renal function such as urinalysis and urine culture, intravenous pyelography, voiding cystourethrography and renal function tests, including blood urea nitrogen, creatinine, and 24-hour creatinine clearance were performed as indicated. When there was evidence of obstructive uropathy, appropriate consultation for cystoscopy was obtained.

Detrusor-Sphincter Syndromes

Utilizing these methods, a number of specific syndromes involving detrusor sphincter dysfunction were delineated. Although there was some overlap among syndromes, they were helpful in directing therapeutic efforts.

Syndrome of Detrusor Hyperreflexia

This was defined as an involuntary detrusor contraction at a low volume of bladder filling (Figure 1). This cystometric finding was associated with one of three types of sphincter function:

1. Normal supraspinal innervation of the external urinary sphincter. The patients in this group could contract the sphincters with either an empty or full bladder. They had histories of urinary frequency and urgency, but rarely of incontinence.
2. Uninhibited sphincter relaxation. These patients demonstrated a volitional inability to contract the sphincters usually with an empty, but occasionally only demonstrable with a full bladder or during a detrusor reflex. Complaints were usually those of urinary incontinence sometimes related to sudden changes in posture.
3. Detrusor-sphincter dyssynergia. Electromyography reveals clonic activity of the sphincter during a detrusor contraction. These patients suffer from frequency, urgency, and incontinence and frequently have difficulty initiating micturition.

Effective treatment of the syndrome of detrusor hyperreflexia must reduce the hyperactivity of the detrusor muscle. Initially, attempts were made with medications including anticholinergics and ganglion blocking agents. The difficulty with these medications was that although urinary frequency was decreased, residual urine volumes tended to increase, and urgency persisted.

Sacral nerve blocks were carried out in many patients to determine which of the sacral nerves were operative in detrusor reflex activity.[10] This was done by blocking sequentially the nerves with local anesthesia using cystometrogram control to determine when the detrusor reflex was abolished and bladder capacity significantly increased (Figure 3). If this could be accomplished by anesthetizing one or two sacral nerves the patient was considered a candidate for selective differential sacral rhizotomy.[11,12] Using the operating microscope, the individual fascicles of the selected sacral roots were in turn stimulated and anesthetized to identify fibers which innervate the bladder only. These were then sectioned, leaving the remainder of the nerve intact. We were thus able to restore more physiologic voiding for the patient by preserving the detrusor reflex and sphincter function, but at the same time increasing bladder capacity. We have had no difficulty postoperatively with disturbance in sexual function.

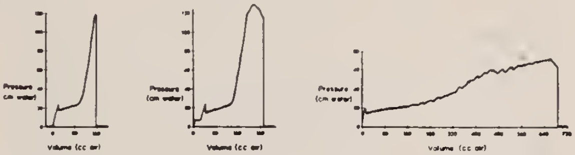

Fig. 3—Cystometric response following sacral nerve blocks. Left: Control cystometrogram showing low threshold detrusor hyperreflexia. Center: Cystometrogram following a unilateral S-3 block showing little change. Right: Cystometrogram following unilateral S-3 and S-4 blocks showing abolition of the detrusor reflex response.

If surgery was not deemed advisable, consideration was given to a more permanent sacral nerve block using phenol or a radio-frequency thermal lesion. If multiple sacral roots appeared functionally operative in detrusor innervation making permanent sacral blocks or rhizotomy impossible, repeated instillations of pontocaine into the bladder were performed. This appeared to reduce the sensation of urgency although the cystometrogram did not always change significantly.

If incontinence remained a significant problem after detrusor hyperreflexia had been effectively treated, implantation of an artificial urinary sphincter was considered.[14] This silicone rubber prosthetic urinary sphincter is comprised of four principal parts: (1) a fluid reservoir, (2) an inflatable occlusive cuff, and (3) an inflating pumping mechanism, and (4) a deflating pumping mechanism (Figure 4). The cuff encircles the urethra in such a manner that when completely inflated the urethra was occluded. The reservoir contained a radiopaque fluid, sodium diatrozoate, which was utilized to inflate the cuff. The pumping mechanism was activated by squeezing a bulb which was placed subcutaneously in the labia or scrotum. The pumping mechanism contained valves which controlled the maximum pressure which could be exerted inside the cuff, preventing possible overinflation. Activation of the deflating pumping mechanism by squeezing the other subcutaneous bulb opened the urethral cuff by returning fluid from the urethral cuff to the reservoir; with cuff opening unimpeded voiding occurs.

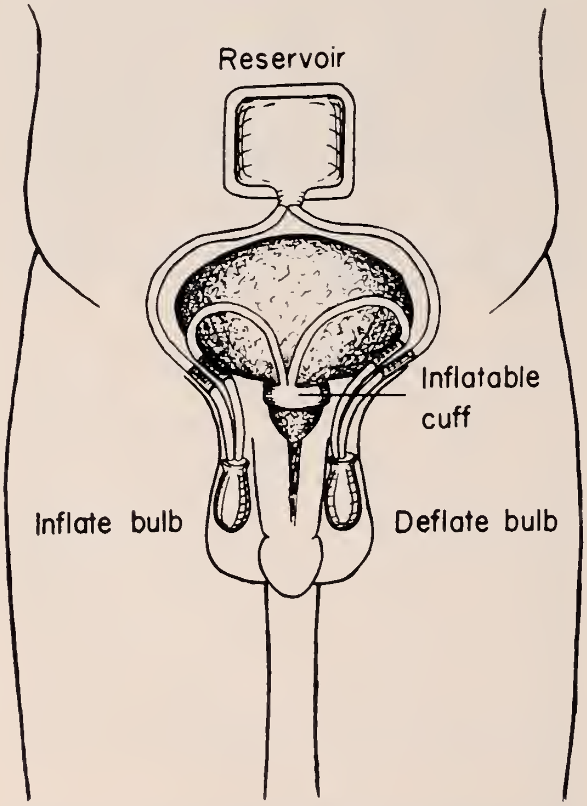

Fig. 4—Diagram of prosthetic urinary sphincter consisting of four principal parts: reservoir, inflatable cuff, and an inflating and deflating pump mechanism.

Syndrome of Detrusor Areflexia

This diagnosis was made when detrusor reflex could not be induced on the cystometrogram even after the subcutaneous administration of Bethanechol Chloride (Urecholine). Before making secondary causes of areflexia such as the administration of atropine-like substances, for example, phenothiazines and belladonna derivatives. Areflexia can also result from infection, overdistension, or chronic catheter drainage of the urinary bladder. The administration of urecholine subcutaneously will frequently induce a detrusor contraction on the cystometrogram in these cases of areflexia due to "local" causes. In addition, the normal person can suppress the detrusor reflex and often does in the examination environment.

The following sphincter abnormalities have been noted to be associated with detrusor areflexia:

1. Normal sphincter innervation with vesical paresthesiae. The cystometrogram of these patients was marked by severe urgency at low-filling volumes, areflexia, and intact supraspinal sphincter innervation. Any instrumentation in the urethra produced intense paresthesiae and urgency to void. Patients with this syndrome gave histories of

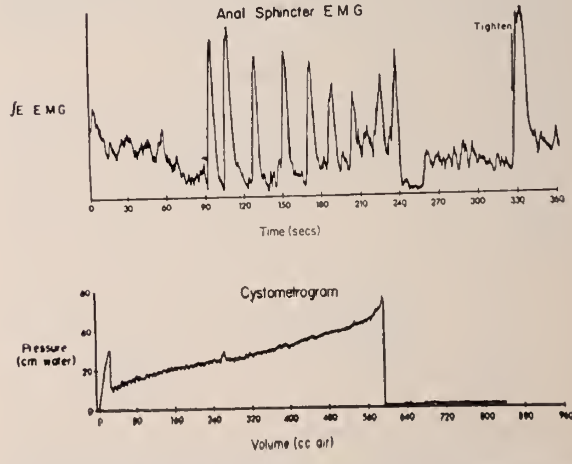

Fig. 5—Clonic sphincter activity with detrusor areflexia and increasing bladder distension.

painful urgency and frequency without urinary incontinence.

2. Detrusor areflexia with uninhibited sphincter relaxation. Electromyography of voiding revealed an inability to voluntarily contract the sphincters with increasing bladder distension. These patients gave a history of sudden episodes of urinary incontinence without prior sensation of urgency.
3. Detrusor areflexia with clonic sphincter activity (Figure 5). With increasing bladder distension, uncontrollable clonic activity was induced in the sphincter muscle. These patients gave a history of urinary retention.

Treatment of patients with detrusor areflexia was directed toward achieving satisfactory emptying of the urinary bladder. Occasionally, parasympathomimetic drugs such as urecholine and prostigmine were useful. Intermittent self-catheterization can permit the patient periodically to completely drain his bladder and to check his own residual urine volume.[9] This technique was easily done especially in the female and in our experience infection has been less of a problem than with continuous catheter drainage.

Topical instillation of tetracaine hydrochloride (pontocaine) has been helpful in patients with urethra and vesical paresthesiae. In a few selected patients with severe difficulty, appropriate sympathectomy has been effective in relieving symptoms. It is known that the bladder neck and urethra have a rich sympathetic supply.

If there appears to be complete denervation of the bladder on testing and the patient has complete inability to void, a detrusor stimulator was considered. Although some problems remain to be solved with this device, it can be clinically effective in carefully selected patients.[6] When incontinence is a significant problem, implantation of an artificial urinary sphincter can be carried out.[14]

Summary

We have attempted to outline our diagnostic and therapeutic approach to patients with neurologic urinary bladder dysfunction. This remains a very difficult and occasionally baffling problem. We are hopeful, however, that a multidisciplinary approach will increase our understanding of the complexities involved and thereby improve our therapeutic attempts.

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Continuing Medical Education

Special Socio-Economic Conference

The Minnesota State Medical Association has scheduled a special Socio-Economic Conference for November 18-19, 1976 at the Thunderbird Motel, Bloomington, Minnesota. The Conference will precede the opening of the MSMA House of Delegates on November 19 at the Registry Hotel.

The Conference program will feature Economist Joseph P. Newhouse, Ph.D. and another speaker of national prominence. Participants will have an opportunity to zero in on three major socio-economic topics: (1) State Legislation, (2) Health Planning, (3) Health Delivery & Third Party Relationship.

Dr. Newhouse will address a breakfast session at 7:30 a.m. on Friday, November 19.

Registration information and other details will be published in the next issue of

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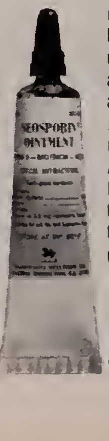
Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing. **CONTRAINDICATIONS:** Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components. **WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended. **PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. **ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



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MSMA Highlights

The Mystery of Medicaid

A recent survey of Minnesota State Medical Association (MSMA) members concerning the Minnesota Medical Assistance Program (Medicaid) elicited a response representing approximately 50% of the practicing physicians in Minnesota. This excellent response provides a solid data base on which to work with the Minnesota Department of Public Welfare (DPW) to enhance the physician's ability to devote his time primarily to providing quality medical care to the financially needy patient rather than to the administrative activities involved in receiving payment for the care provided.

Seemingly endless forms, bookkeeping tangles, and unreturned phone calls often obscure the fact that Minnesota's Medicaid program is one of the best developed in the nation, and one of the few which provides to recipients the full range of medical services available under the program. California, New York, and others look with envy upon this Medicaid paradise in the Midwest. The federal government considers Minnesota a model program and DPW reports that about half of the programs in the country have contacted them to find out what Minnesota is doing that is so right. Despite such accolades from coast to coast, the survey of Minnesota physicians has identified specific areas in the state system which demand modification.

MSMA's Committee on Medical Service is a major component of the new Association's Division of Socio-Economic Affairs (DSEA). The Committee is charged with the responsibility for seeking to implement measures which will bring about the necessary modifications within the system.

Encouragingly, the majority of solutions to the concerns identified do not appear to constitute major reforms to the system, nor are they prohibited by law. Based on survey results, physician receipt of properly identified, correctly calculated payments within a reasonable period of time and access to necessary information with a minimum of frustration on a current basis represent the major objectives which must be realized to achieve a smoothly functioning system.

The Department of Socio-Economic Research of the DSEA is charged with responsibility for staffing the Committee on Medical Service. The Committee is responsible for liaison with the Department of Public Welfare and with staff is communicating on a daily basis with staff members at DPW. Commissioner Vera J. Likins and Deputy Commissioner James J. Hiniker have met with the Committee on Medical Service to explore mutual concerns. Mr. Hiniker has recently been appointed official liaison from DPW to the MSMA and has proven himself to be readily available for consultation.

Internally, DPW has established an intensified training program for its own staff to familiarize them with intricacies of the Minnesota Relative Value Index and to enable them to provide prompt answers to physician inquiries. Currently, plans are being made by DPW to upgrade their training program for physician office personnel and MSMA staff is being consulted regarding such plans. The post of Director of the Medical Assistance Program, vacant since December, 1975, has been filled. Current indications make apparent the likelihood of a stronger liaison relaionship in the months ahead.

Paramount to success in the continuing liaison effort with the Department of Public Welfare is accurate and current information. The MSMA Committee on Medical Service invites physicians to contact Association headquarters to convey concerns or request information regarding the Minnesota Medical Assistance Program.

Address your communication to the MSMA Division of Socio-Economic Affairs, Suite 900, American National Bank Building, St. Paul 55101.

Some Questions and Answers Relating to the Medicaid Program

What is the Medicaid program and where did it come from?

The Medical Assistance Program (Medicaid) was created by the same act of Congress which established Medicare. Known as the "Social Security Amendments of 1965," Public Law 89-97 added a section designated Title XIX to the United States Social Security Act (SSA). Medicare was established by addition of Title XVIII to the SSA.

The stated purpose of the Medicaid program is to enable "each State, as far as practicable under the conditions in such State, to furnish: (1) medical assistance on behalf of families with dependent children and of aged, blind, or permanently disabled individuals, whose income and resources are insufficient to meet the costs of necessary medical services, and (2) rehabilitation and other services to help such families and individuals attain or retain capability for independence or self-care . . ."

Provisions in federal law are often very general. Are there any federal controls on Medicaid in addition to the federal law?

Yes. The federal law authorizes the Secretary of the U.S. Dept. of Health, Education and Welfare to promulgate regulations for administration of the program. When adopted, such regulations have the force and effect of law. These regulations are published as Title 45 of the Code of Federal Regulations (45 CFR).

Are there any state level controls on Medicaid in Minnesota?

Yes. Chapter 256B of the Minnesota Statutes declares medical assistance for the needy to be a matter of state concern and establishes a statewide program of medical assistance with free choice of vendor. In addition, the state agency administering Medicaid (DPW) is directed to promulgate rules and regulations to carry out the provisions of Chapter 256B. The major regulation governing Medicaid at the state level is DPW Rule 47.

With all of the rules and regulations at different levels of government, how it is possible to determine which takes precedence if conflicting provisions should be discovered?

Precedence for all Medicaid laws and regulations is well established. Federal statutes are the chief precedent superseded only by the Constitution of the United States. Federal regulations may not contradict federal law and may not exceed the authority provided by federal law. State laws are next in priority followed by state regulations.

Why can't the Minnesota State Medical Association negotiate to raise Medicaid reimbursement levels?

Reimbursement levels for Medicaid are governed by federal statute. The Social Security Amendments of 1972 restricted Medicaid reimbursement to Medicare levels. Medicare may not pay more than the 75th percentile of usual and customary for any given procedure. A significant number of states have reimbursement levels much lower than those in Minnesota. A current U.S. Senate bill, known as the Talmadge amendments, which is described below would significantly change determination of reimbursement levels by further reducing them.

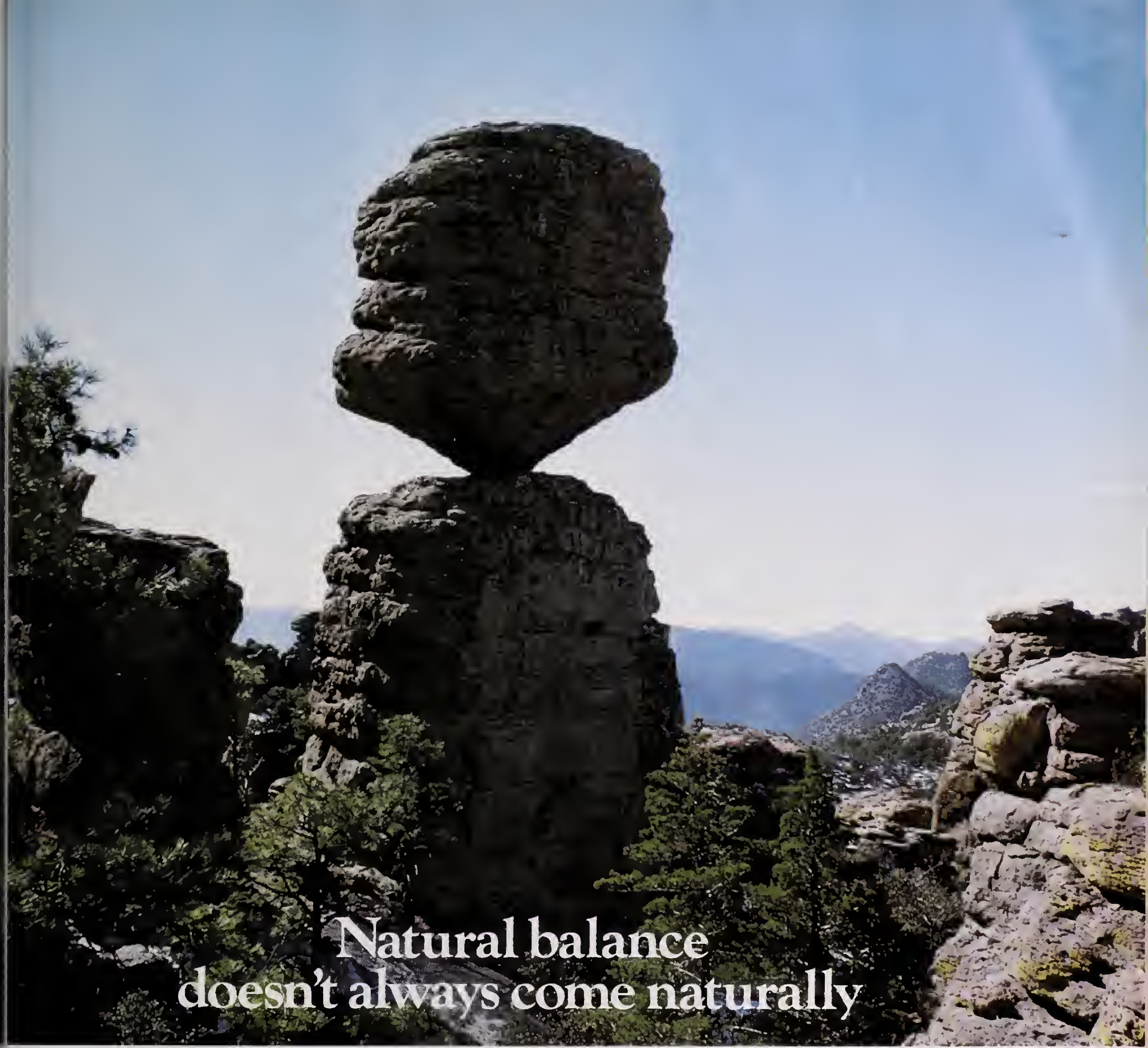
Are any of the Medicaid laws or regulations subject to revision and may organized medicine participate in the revision process?

Medicaid laws are subject to revision by Congress or by the state legislature depending on their body of origin. Organized medicine continually participates in this revision process. Currently Congress is considering a bill entitled the Medicare-Medicaid Administrative and Reimbursement Reform Act (S. 3205) introduced by Senator Herman Talmadge of Georgia. As introduced, this bill provides for extensive changes in the Medicare and Medicaid programs. The AMA is actively involved in Congressional consideration of the Talmadge amendments. Through communications with Minnesota congressmen and through the AMA the MSMA participates in issues at the Congressional level.

By subscribing to the Federal Register, a government publication, MSMA is informed daily of proposed federal regulations. When MSMA members may be affected by such proposed regulations the Division of Socio-Economic Affairs prepares comments based on factual research data for response to the federal agency involved, usually HEW.

At the state level MSMA energetically participates in legislative and regulatory processes, seeking out the law and rule makers, defining the issues, providing background material and making recommendations. A recent example involved proposed revisions to DPW Rule 47 which governs Medicaid in Minnesota. Several Association committees, legal counsel and the Department of Socio-Economic Research participated in analyzing this 39-page document and preparing recommendations which were presented by Dr. Richard E. Anonsen, President, at a public hearing. Present information indicates that the majority of MSMA's recommendations will be accepted and will be part of the revised document. The State Register, a weekly publication, provides notice of proposed state regulations.

If you have specific questions or problems concerning the Minnesota Medical Assistance Program, please call or write the Division of Socio-Economic Affairs, Minnesota State Medical Association, Suite 900 American National Bank Building, St. Paul, MN 55101. (612) 222-6366.



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WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

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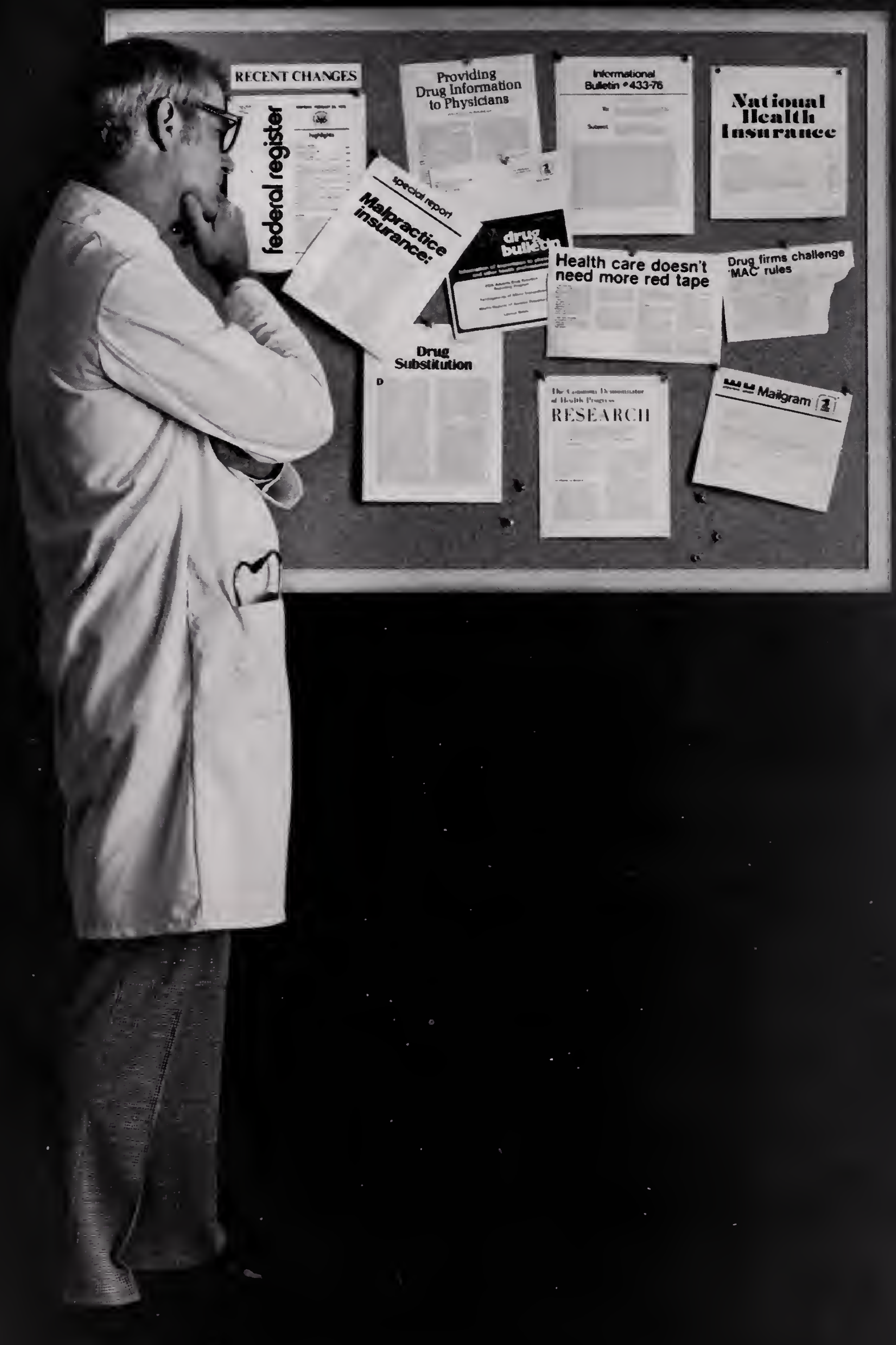
RECENT CHANGES
federal register
Providing Drug Information to Physicians
Informational Bulletin #433-76
National Health Insurance
special report
Malpractice insurance:
drug bulletin
Health care doesn't need more red tape
Drug firms challenge 'MAC' rules
Drug Substitution
RESEARCH
Mailgram

THERE ARE A LOT OF PEOPLE GETTING BETWEEN YOU AND YOUR PATIENT.

Medicine today is in the spotlight, subjected to all inds of scrutiny. Your control over patient therapy is eing monitored, judged and occasionally abrogated, ometimes by unknown third parties.

The worry is that in the wake of this focus, the rela- ionship between you and your patient will be weakened, ithout offsetting benefits. Consider three examples:

Drug substitution In most states, pharmacy laws, egulations or professional custom stipulate that your on-generic prescriptions be filled with the precise prod- cts you prescribe. But in the last five years, a dozen or ore State laws have been changed, permitting the phar- acist in most cases to select a product of the same eneric drug to fill any prescription.

Ironically, this dilution of physician control has aken place against a background of growing evidence at purportedly equivalent drug products may be in- uivalent, since neither present drug standards nor their nforcement are optimal. In fact, the FDA itself says it as not enforced the same standards for hundreds of follow-on" products that it had applied to the original DA approvals. Thus physician control over patient erapy is being eroded with a risk that patients may be posed to drugs of uncertain quality.

The major advertised claim for substitution is reduced rescription prices for consumers. Yet no documentation any significant savings has been produced.

MAC Maximum Allowable Cost, MAC for short, is Federal regulation designed to cut the Government's rug bill by setting price ceilings for drugs dispensed to edicare and Medicaid patients. Unless the prescriber rtifies on the prescription that a particular product is edically necessary, the Government intends to pay only r the cost of the lowest-priced, purportedly-equivalent, generally-available product. The effect of the program may be that elderly and indigent patients will be restricted to products which someone in Washington believes are priced right. Practicing doctors will have little to say about administration of the program, since Government will have absolute authority to make its choices stick.

The drug lag The future of drug and device research depends upon a scientific and regulatory environment that encourages therapeutic innovations. The American pharmaceutical industry annually is spending more than $1 billion of its own funds and evaluating more than 1,200 investigational compounds in clinical research. Disease targets include cancer, atherosclerosis, viruses and central nervous system disorders, among others. But there is a major barrier to the flow of new drugs to your patients: The cost of the research is more than ten times what it was, per product, in 1962; and whereas governmental clearance of new drug applications took six months then, it commonly consumes two years now.

The FDA needs adequate time, of course, to consider data. But it is equally clear that the present approval process contributes to needless delay of needed therapy. That's why the increased efficiency of the drug approval process is vital to all our futures.

If these issues concern you, we suggest that you make your voice heard—among your colleagues and your representatives in State legislatures and in Washington.

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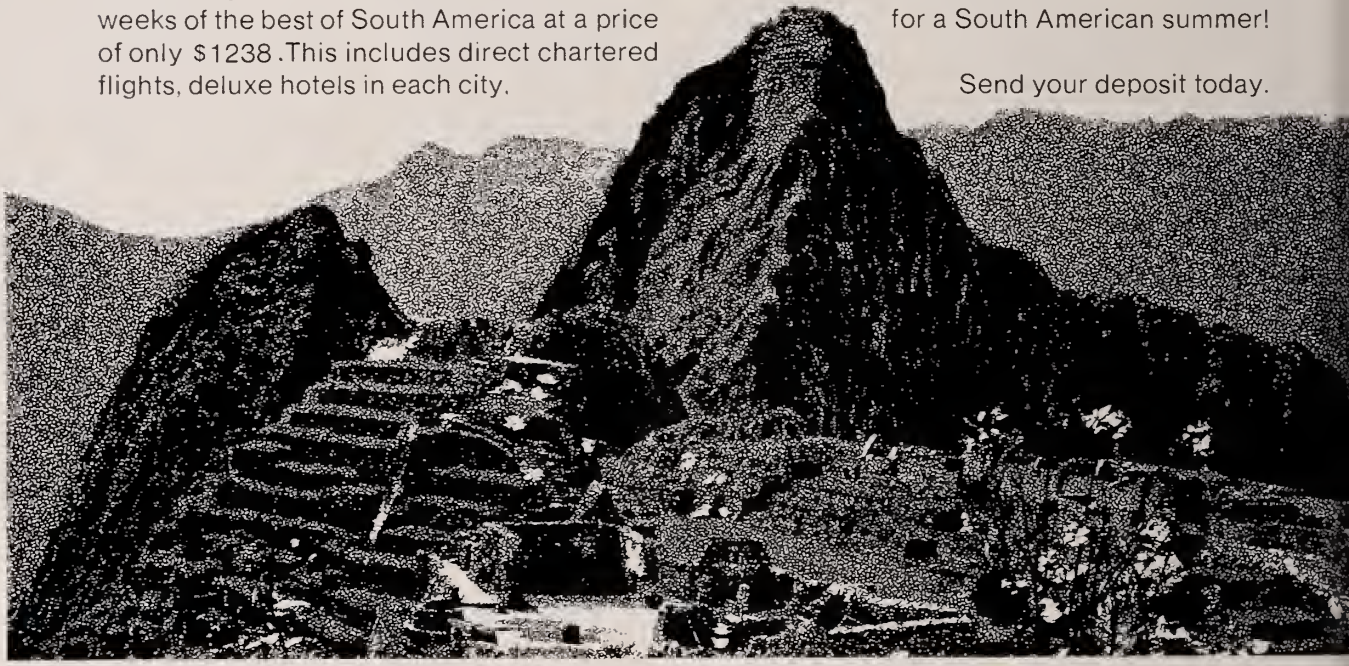

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Editorials

Reduction Mammoplasty

THE BREAST REDUCTION procedure described by Rice is somewhat different from the conventional operations used to decrease breast size. Basically, the procedure is an adenomammectomy, but leaving the breast flaps substantially thicker. To eliminate some of the redundancy of skin, the lower incision margin is transferred to the lower level. The text states that this excision of skin below the inframammary fold incision is 2-4 centimeters and Figure 5B indicates 2.5 inches.

The advantages of this procedure suggested by the author, I believe are valid. It appears that the submammary scars can be kept shorter than in the usual reduction operation. Also, the procedure eliminates the scarring on the surface, the breast, and about the areola. The risk of compromise of the blood supply to the nipple-areola complex would appear to be small. It appears that this procedure would be most useful for a tense fatty breast with little sagging, or for a breast with only moderate enlargement.

The disadvantages of this procedure have not been mentioned. Most reduction mammoplasties are carried out to make the breast smaller and thus relieve weight on the neck and shoulders. The weight of the tissue removed in the two cases described is substantially less than what is removed with the usual breast reduction. Also the postoperative photographs indicate the breast is quite flat and the nipple and remaining breast are lower on the chest wall. For the patient with large, pendulous, heavy breasts, the nipple-areola complex often descends 6-10 centimeters. In the usual breast reduction procedure, the nipple is returned to a more pleasing height, the remaining breast protrudes outward from the chest wall, resulting in a breast simulating that of a young person. This is done at the expense of some scarring about the areola and immediately below it.

Lyle V. Kragh, M.D.
Minneapolis, Minnesota

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*See page 707.

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Letter to the Editor

Dear Editor:

Minnesota Clean Indoor Air Act

August marks the one year anniversary of the Minnesota Clean Indoor Air Act. This act has provided tremendous potential benefit for all of our patients as it means that there is now a law which limits smoking to designated areas. In my activities throughout the Twin Cities, it is apparent that knowledge of this law and enforcement of this law varies from place to place. It is obvious that certain restaurants and other establishments have been reluctant to enforce it at the risk of losing some of their customers; however, it is also obvious from those establishments which have implemented the law that it has certainly worked out to their advantage.

However, I have been disappointed with the compliance of this law in our hospitals, and I would hope that all physicians throughout the state, whether they smoke or not, will realize the potential problem that this could create for some of their patients and urge the administrators of the hospitals in which they work, and urge their patients in their own waiting rooms, to comply with the requirements which are in the best interest of all concerned.

Minnesota can claim much credit, as was recently acknowledged by the AMA House of Delegates, for this law, and it is now up to all of us to make sure that it becomes widely practiced and sensibly enforced.

C. Richard Guiton, M.D.
St. Paul, Minnesota

Fractures and Dislocations of the Spine—Bradford and Thompson (page 720).

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Physicians Take Note

Dispense as Written (DAW) Needed on Prescriptions to Preclude Substitution

Physicians are reminded that the 1975 Legislature enacted a new law, Chapter 101, authorizing generic drug substitution under certain conditions. Responding to this new legislation the 1975 AMA House of Delegates passed the following resolution:

"Physicians are again urged to write 'Dispense as Written' or 'D.A.W.' (this must be written in the physician's handwriting) on a prescription when in the physician's professional judgment the patient's health and welfare might be compromised by the substitution of another medication for that which he has specifically identified on his prescription."

The law provides that a pharmacist who receives a prescription for a brand name drug, may, with written or verbal consent of the purchaser, dispense any drug generically equivalent to the brand name prescribed unless the above procedure is followed.

Chester A. Anderson, M.D.
Chairman
Legislative Committee

Minnesota State Board of Medical Examiners

1976 Minnesota Session Laws Chapter No. 222 provides as follows:

Section 40. Minnesota Statutes 1974, Chapter 147, is amended by adding a section to read:

(147.074) (Filing of hospitals served) *Each physician shall file with the board a list of the in-patient and out-patient medical care facilities at which they have medical privileges. This list shall be updated when the physician applies for license renewal.*

This list must be submitted to the Board with your 1977 annual registration payment. Forms will be mailed to you with the annual registration renewal form.

Loren E. Nelson, M.D.
Secretary-Treasurer

Medical Alumni of Hennepin County Medical Center

A reunion of all medical alumni of Hennepin County Medical Center (Minneapolis General Hospital, Hennepin County General Hospital) will be held in Minneapolis October 14, 15 and 16, 1976. For information, write to Eldon Berglund, M.D., Hennepin County Medical Center, Minneapolis, Minnesota 55415.

WE NEED YOU

Every once in a while a cause of unusual merit comes along. Such a one is the drive to increase the resources of the Minnesota State Medical Association Foundation Student Loan Fund.

For more than 15 years this Foundation's activity has given witness to the interest of practicing physicians in those who will one day stand in their shoes. We can all take pride in the record.

Two hundred twelve interest-free loans have been provided to needy students. We can all be proud of the default-free record of repayment by the young people who have been aided by the M.S.M.A.

Bad times have come upon the fund, for while these loans do draw interest after graduation and the fund assets do grow slowly, the need for student assistance grows more rapidly. Everything is up: tuition, books, fees, living costs . . . everything but student financial support. As many of the traditional sources of aid have eroded, more students are turning to their seniors in the profession to help them through their training period. As a result your fund assets are completely disbursed in student loans.

Currently, thirty medical students have applied for assistance and more, we are certain, will be along later. Many will not be accommodated unless the resources of this fund are augmented.

If every Minnesota physician made a tax deductible contribution of $100 to the M.S.M.A. Foundation Student Loan Fund, the problem would be solved. The worthy young men and women who so badly need our help would find a ready and understanding ally.

An organized drive is underway. YOUR HELP IS NEEDED. Contribute today and contribute generously.

John Regan, M.D.
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PAGE 705-706 [illegible]

Special Article

Reduction Mammoplasty

CARL O. RICE, M.D.*

Reduction Mammoplasty for heavy, painful breasts can be accomplished without nipple transplant, and essentially without scar. The technique must be meticulously adhered to.

REDUCTION MAMMOPLASTY, by the method which I shall now describe, was a fortuitous serendipity originating from adenomammectomy.† Instead of leaving a host of scars and a hazardous transplantation of the nipple, reduction mammoplasty by this method leaves an essentially scarless breast.

The enormously large breasts with which some women are handicapped are not always due to hypertrophy of the breast substance, but to an over-abundance of fat, fibrous plaques, strands of interstitial tissue, islands of cellular infiltration, and a minimal amount of breast and/or ductal epithelium. The reason for this is not clear. If, on the other hand, the male breast becomes abnormally large, the breast substance does undergo hypertrophy and hyperplasia.

When we reflect the predeliction of the human body to deposit fat at various anatomical areas, we find some with large amounts of fat on the arms, but none on the forearms; subcutaneous fat in the abdominal wall, or the omentum may take over this burden; in others there are those who have bulges in the thighs, the gluteal regions, the dromedary hump at the cervico-dorsal area, or in the supraclavicular hollows. Only a few individuals deposit their surplus fat uniformly throughout the body.

I speculate that some women with enormous breasts have this inexplicable characteristic within their breast. The major portion of the enlarged breast of a woman often consists of fat tissue, and in many instances I have observed this fat to have the characteristics of a coelescent lipoma: the fat cells of which appear grossly larger than the fat cells of the adjacent subcutaneous fat, and though there is no true capsule, the large fat lobules seem to shell out like a loculated lipoma. In a few instances, after doing adenomammectomy on a large, fatty breast, recurrence has proven to be fat tissue with the large cell characteristic of a lipoma; furthermore, many otherwise well-proportioned women have very large breasts and are unable to reduce them by weight reduction.

Currently, the mode in breasts is moderate, within a cup size from A to B, and possibly C. D, E and F are out!

Adenomammectomy was developed in 1951*, and was at that time designed for the purpose of removing multiple areas of fibrocystic disease in order to eliminate the need for repeated operations. From that procedure, reduction mammoplasty had its origin. Over a period of six or eight years numerous modifications were tried and rejected. To that extent a meticulous technique must be adhered to, as described in the following paragraphs.

The Incision

A mammary thoracic fold incision is made with a sharp scalpel, cautiously guarding against crossing the natural folds of the skin, lest a broad or thickened scar results.

The Adenomammectomy

After the skin incision has been made with the scalpel, and to diminish bleeding, the combined coagulating-cutting endotherm blade is used to dissect the breast from the pectoral fascia. To cut the pectoral fascia and enter the muscle at any point increases the bleeding and the hazards of subsequent oozing. The dissection continues cephelad to the upper limits of the breast substance (Figure 1).

The surgeon's left hand then everts the breast substance and a row of Kocher forceps is applied

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*Editor Emeritus, Minnesota Medicine, Minneapolis, Minnesota.
†Surg, Gynec, Obstet 93:759, 1951.
See editorial, page 699.

to the uppermost portion of the breast to be used for traction as well as identification. The breast substance is then dissected from the subcutaneous fat with a sharp scalpel, leaving one or two millimeters thickness of the so-called "breast capsule," adjacent to the subcutaneous fat. (There is no true breast capsule, but the line of demarkation—not a plane of dissection—at this point is detectable.) The dissection returns toward the starting point, shaving as close to the subcutaneous fat as possible (Figure 2). A sharp scalpel is preferred at this point rather than the endotherm cutting-coagulating blade, because a burn with the coagulator, inadvertently contacting the back side of the skin, would produce a scar on the surface of the breast.

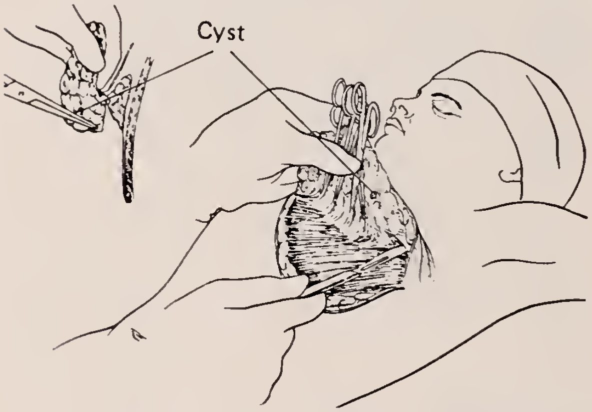


Fig. 1—The dissection of the breast from the skin is being carried out. The insert shows a small portion of breast tissue has been cut across in the upper area. (See Figure 3 for additional trimming; also see paragraphs on "Identifying the Remaining Breast Tissue.")

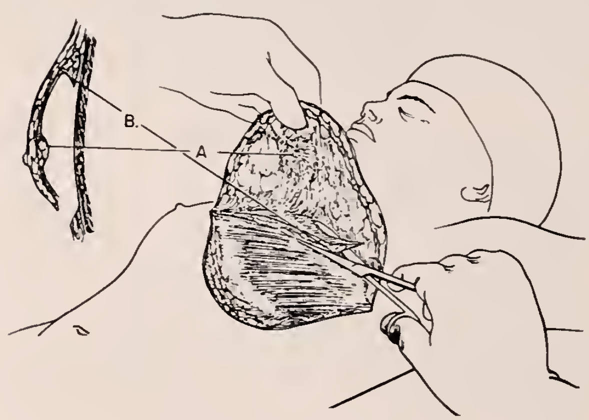


Fig. 2—The removal of the breast substance has been completed. A and B show additional trimming of the excess breast tissue that has been left behind, in order to provide a smooth contour.

Identifying Inadequate Removal of Breast Tissue

As much of the breast substance is dissected away en masse as possible. Occasionally, because of a slight loss of orientation, one may leave an excessive amount of breast substance here and there with the subcutaneous fat. This can be identified, after the major mass of breast substance has been removed, by returning the breast flap to the chest wall and stroking across it with a moist, gloved palm, which readily identifies irregular masses (Figure 3). These irregular masses can be trimmed with a shaving stroke of a scalpel, or with a curved shears. Leaving a small edge of the upper breast margin, the most often encountered residue, can be identified as a ridge. This ridge must be removed lest, after healing has occurred, it is identified incorrectly as a mass or a regrowth of tissue.

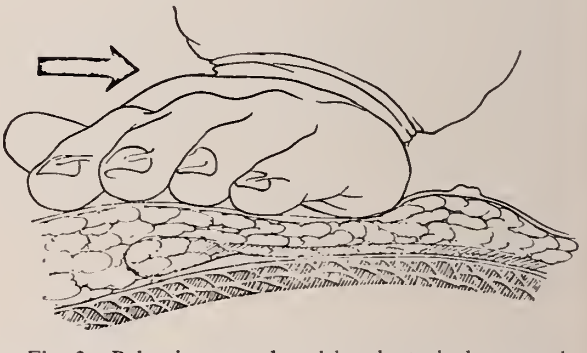


Fig. 3—Palpating wet gloved hand, stroked across the breast, identifies excessive breast substances.

The Reduction Mammoplasty

The adenomammectomy has now been performed, leaving only a narrow band of "breast capsule," uniformly distributed throughout the under-surface of the breast flap. From a large breast, 250 to 400 grams of breast substance will be removed. (The average B-sized breast contains only 50-60 grams of breast tissue. The major portion of the delightful contour of a breast is subcutaneous fat.)

Eliminating Redundancy

In order to eliminate the redundancy which remains after the adenomammectomy has been done, the flap of breast is pulled over the incision, so as to indicate the approximate point at which additional skin is to be removed from the abdominal wall (Figure 4). An ellipse of skin, from two to four centimeters, at the widest point, is removed. To remove the redundant tissue from the breast flap instead of the abdominal wall results in turning the nipjple to an undesirable underneath position (Figure 4-B).

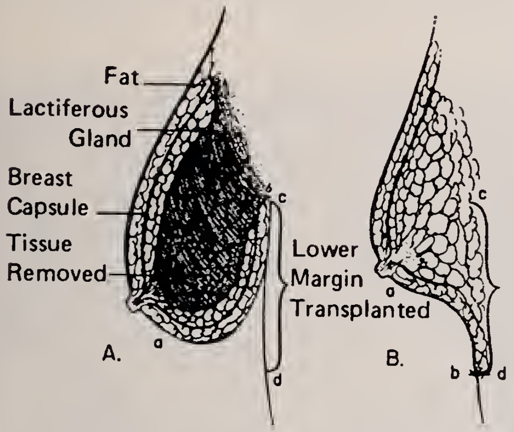


Fig. 4—"A" shows area of breast substance removed. "c-d" shows area where skin was removed from chest wall, as illustrated in Figure 5, and replacement of redundant undersurface of breast, "a-b," onto the chest wall, closing, "c-d" as illustrated in "B" and in Figure 5. This accomplishes the reduction mammoplasty as shown in "B." Bandaging the breast upward allows the reduced breast to heal in a high position.

Control the Oozing

The bleeding surface of the remaining "breast capsule" must now be meticulously dry. This is done with the coagulating blade of the endotherm. Catgut, or other sutures, are not used, for they are time-consuming and leave foreign material, around which a giant cell reaction may form. The coagulated tissue causes less foreign body and exudative reaction.

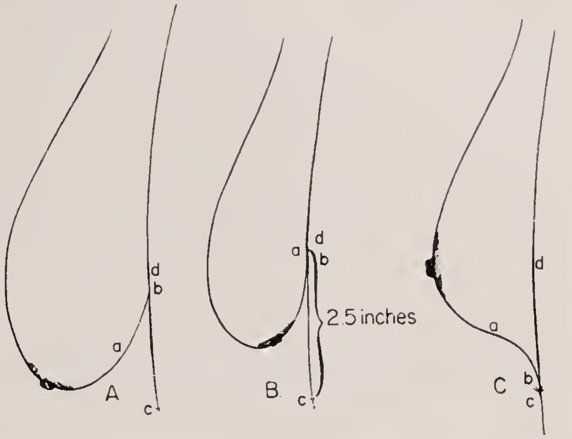
Bilateral adenomammectomy is done before closing the wound.

Closing the Incision

Before suturing the two skin edges with lock stitches, two Shirley-type suction tubes* are placed under the breast flap and brought out through the incision. They are anchored with a stitch. Sixty millimeters of negative water pressure are applied, so as to keep the exudate from accumulating under the breast flap. The tubes are occasionally irrigated with water so as to hemolize the blood that may have lodged within the tube.

The Dressing

A single Telfa dressing is placed directly upon the incision; over the entire breast a large shield



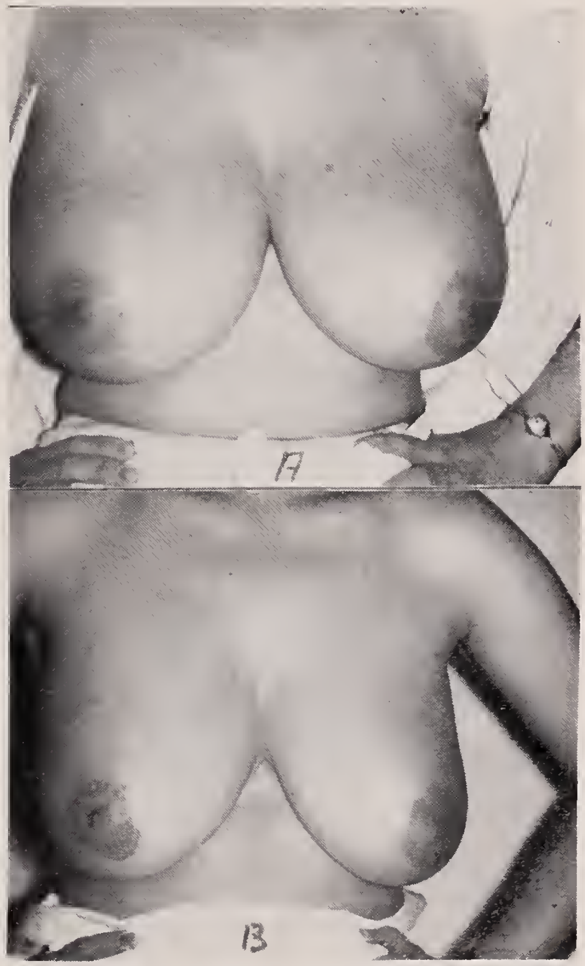


Fig. 5—Female, age 35, breast enlargement, mastodynia. (A) Preoperative. First operation, right breast 210 grams, left breast 165 grams. (B) Six months after second operation, breast right 195 grams, left 170 grams. Total removed: 740 grams.

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*Shirley suction tube is a double tube, the smaller one of which is an air vent, and allows the tube to maintain suction.

of one-half inch rubber sponge is fashioned. A similar rubber sponge shield is made for each breast. This sheet of rubber sponge is smoothly strapped in position with adhesive while the patient is lying supine upon the operating table. This allows for a slightly higher point of adherence onto the pectoral fascia and thereby aids in reducing the redundancy which might otherwise have seemed inevitable.

Twenty-four hours later the adhesive dressing is removed, the wound is inspected, and the rubber sponge re-applied and held in position with two 6-inch Ace bandages. These large rubber sponges will assume the contour of a brassiere cup. This pressure must be maintained for 10 to 14 days. If suction has been effective, the Shirley tubes can be removed at the end of 24 to 48 hours.

Minor Sequel—Complications

Agonizingly meticulous attention to the control of minor oozing usually rewards the surgeon with primary healing. When the rubber sponge brassiere dressing is finally removed, the higher adherence of the breast flap gradually sags into a normal, graceful contour with minimal irregularities. This period of restoration will require four to six months.

In some instances fluid exudate may accumulate under the breast flap, and this can be removed with an aspirating needle. If a blood clot forms under the breast flap, it is best to return the patient to the operating room, remove the blood and resuture the wound, applying the pressure dressings and suction as described above.

Comments

Over the past ten years I have performed at least one hundred reduction mammoplasties, some of which have been done in association with the removal of extensive fibrocystic disease. If mammoplasty had not been performed, these patients would have been left with a long flap-type breast that would not have given the patient the confidence of a good contour. All of the very large breasts can cause discomfort, mastodynia, shoulder-strap pain, and fatigue.

In a half-dozen instances, a second operation has been required, and in these the patient was forewarned.

Figures 5 and 6 indicate the "before" and "after" breast contour.

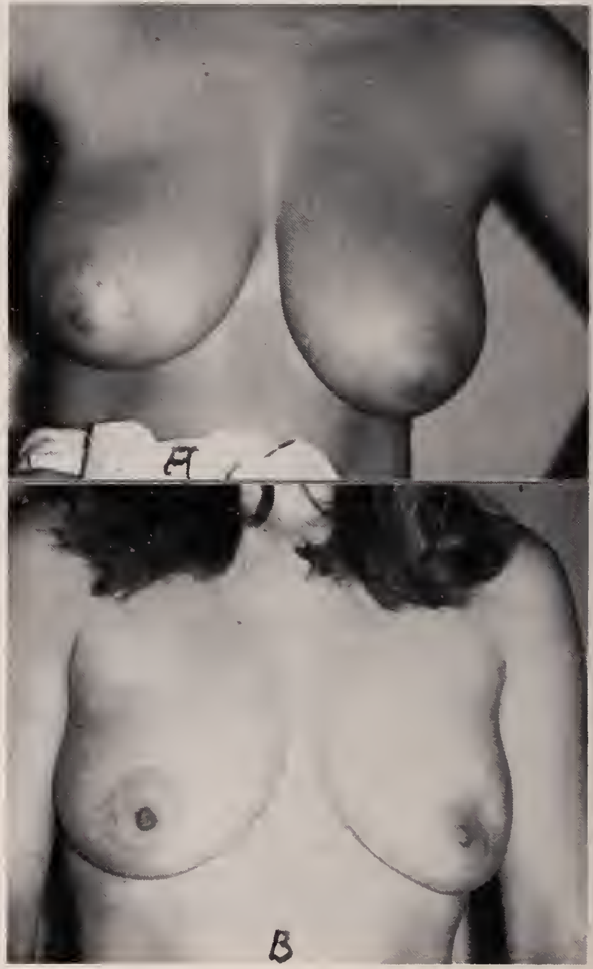

Fig. 6—Female, age 21, mastodynia. Breast enlargement, unhappy with asymmetry and large breasts. (A) Preoperative, note asymmetry. (B) Two years post-op. Total tissue, left 300 grams, right 250 grams.

Reminder: C.M.E. Reports Due

The Minnesota State Medical Association requires triennial reporting of continuing medical education credits as a condition of membership. The current requirement period will end on December 31, 1976. Send in your reports as soon as possible to keep your membership in good standing. Questions: Contact C.M.E. Dept., MSMA, 101 E. 5th St., St. Paul 55101.

Trauma

Fractures and Dislocations of the Spine

Indications for Surgical Intervention

DAVID S. BRADFORD, M.D.* and ROBY C. THOMPSON, M.D.*

This paper classifies cervical and thoracolumbar spine injuries, and provides an approach to surgical management that we have found appropriate and beneficial.

VERTEBRAL COLUMN STABILITY depends on soft tissue support. Posteriorly, the supraspinal and interspinal ligaments, along with posterolateral joints and ligamentum flava provide the "posterior ligament complex." The integrity of this ligament complex is essential for spine stability. Anteriorly, the intervertebral disc, the periosteum, and anterior and posterior longitudinal ligaments also support the vertebral column (Figure 1). One can consider the spine then as two structural columns;[11] an anterior column, consisting of vertebral bodies, discs, and ligaments; and a posterior column consisting of a neural arch, facet joints, and ligaments.

Injuries to the spine may damage one or both of these structural columns, and, in the process, produce spinal instability. It is important to determine whether this instability is acute or chronic. Acute instability implies a fracture that is capable of further displacement soon after injury with immediate neurologic damage. Chronic instability implies an injury that may further angulate, producing greater deformity months or years after injury. Slow and progressive neurologic damage may result from this deformity, but only as a late sequelae from marked angulation. Disruptions of both anterior and posterior columns or disruption of the posterior ligament complex usually results in acute instability. Chronic instability is less common but may result from damage to the anterior column alone over multiple levels (i.e., multiple compression fractures).

Pathomechanics and Classification of Spinal Injury

In considering mechanisms involved in spinal injury, it is useful to describe the relationship of one vertebral segment to another in the conventional X, Y, and Z axis of three dimensional space (Figure 2). Angular motion around the three axis would include flexion/extension, rotation, and lateral bending, while non-angular motion (translation) would include distraction-compression, anterior-posterior shear, and lateral shear. For translation displacement to occur, both structural columns of necessity would be disrupted and acute instability results. Rotational (angular) movements in physiologic range are a normal component in the intact human spine while translational movements are not.

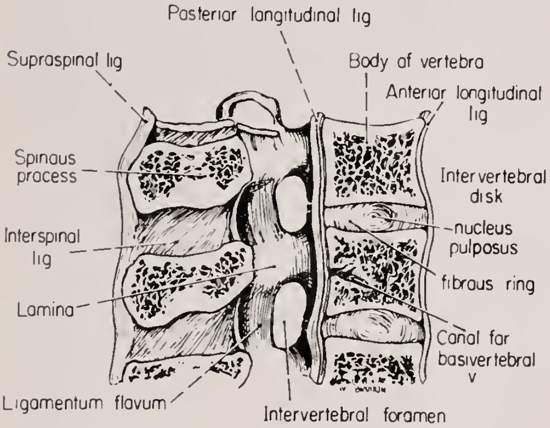

Fig. 1—The vertebral column may be considered as two structural columns; an anterior column consisting of vertebral bodies, discs, and ligaments; and a posterior column consisting of a neural arch, facet joints, and ligaments. (Reprinted from Woodburne, R. T.: Essentials of Human Anatomy. Fig. 12-45. Oxford University Press, New York, New York. By permission.)

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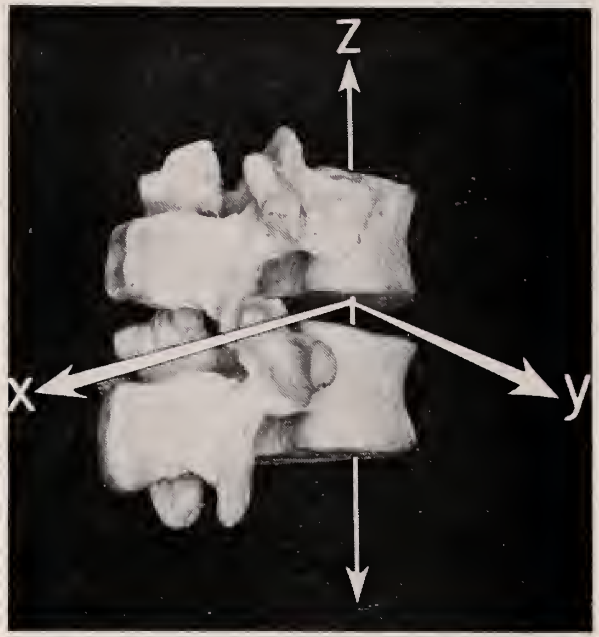


Fig. 2—Mechanisms involved in spinal injury, described as a relationship of one vertebral segment to another in the conventional X, Y, and Z axis. Angular motion is a normal component of the intact spine, whereas non-angular (translational) motion is not. (See text.)

Cervical Spine

Cervical spine injuries will be considered separately from the thoracic and lumbar region because of the degree of mobility present in the cervical spine, and the unique nature of injuries to this area. Forces producing injuries in the cervical spine may be divided into four separate categories, depending upon the position in which the head is held over the neck at the time of injury, and the direction in which the force is transmitted through the cervical spine (Table). Pure flexion injuries rarely produce a fracture or fracture dislocation in the cervical spine because the chin strikes the sternum before damage to bone or soft tissue can occur. However, flexion in combination with compression is a relatively common injury in the cervical spine (Figure 3), and may produce an unstable injury if the posterior soft tissue elements are completely disrupted. When a force transmitted through the neck stops short of disrupting the posterior soft-tissue elements, then a simple compression fracture results. When flexion is combined with rotation, anterior subluxation or facet joint dislocation results (Figure 4). When a compressive force is transmitted down the longitudinal axis of the cervical spine,

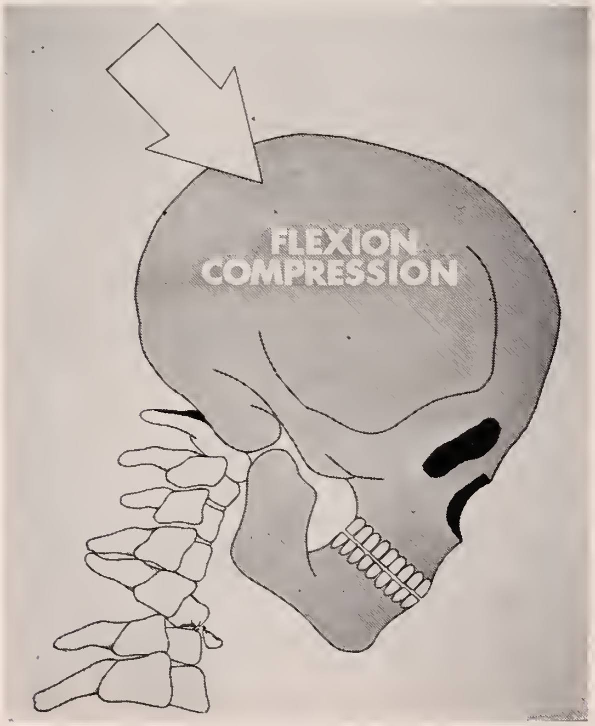


Fig. 3—Flexion compression injuries with disruption of the posterior ligamentous complex usually result in a fracture off the inferior portion of the body above the level of soft tissue disruption. This particular injury is unstable unless it is reduced in traction. When it is reduced, it may go on to spontaneous anterior interbody fusion.

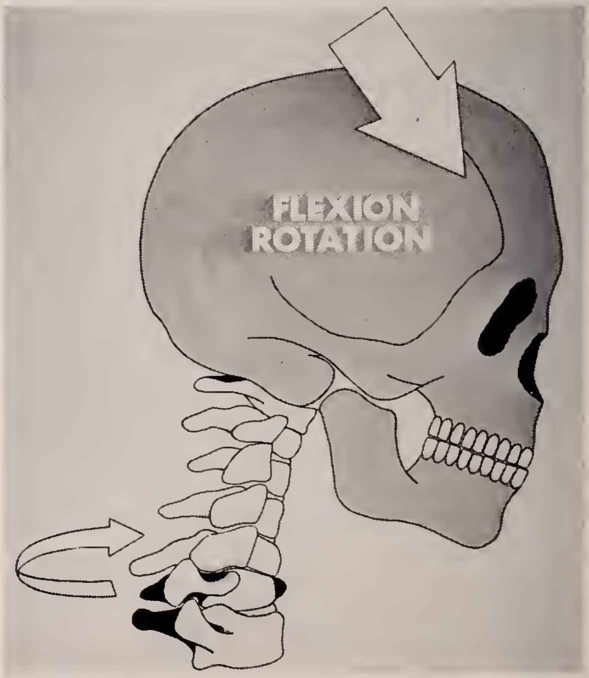


Figure 4—Flexion rotation injuries produce anterior subluxation or facet joint dislocation. These injuries should be reduced in traction. In the presence of a facet joint dislocation as shown, a true lateral of the spine above the level of injury will be seen on the Xray with an oblique view of the vertebra below that level.

a vertical compression load is applied to the vertebral bodies and a bursting type injury occurs. Elements of the vertebral body are then displaced in all directions and, most importantly, posteriorly into the spinal canal (Figure 5). Even though this is an intrinsicly stable injury from the skeletal standpoint, it carries a high incidence of neurologic damage. Extension injuries to the cervical spine do not enjoy the same anatomical protection that the flexion injuries do, since there is no protection when the skull is forced posteriorly, where it may reach the interscapular region. As a result, pure extension forces may produce significant bony and soft tissue injuries to the neck (Figure 6).

The upper cervical spine (occiput—C1-C2) has to be considered separately from the lower five vertebral segments, since the atlanto-axial complex has a different anatomical configuration. Acute flexion forces applied through the upper cervical spine may produce a fracture of the odontoid or a rupture of the transverse ligament of C1. Likewise, acute extension injuries through the atlanto-axial complex may produce a fracture of the base of the odontoid, or disruption of the pars interacticularis of C2 (Hangman's Fracture). Vertical compressive loads may produce a bursting type fracture of the arch of C1 (Jefferson Fracture).

The importance of categorizing injuries to the cervical spine according to the mechanism of injury lies only in the usefulness of this classification in predicting the outcome of the injury. Cheshire,[3] in review of 224 cervical spine injuries classified as above, found that by reducing the injury and holding in skeletal traction, followed by a brace or cast, for a total of 12 weeks, only seven percent of these injuries were unstable. Specifically, he found 95% of vertical compression injuries to be stable, 93% of the facet joint

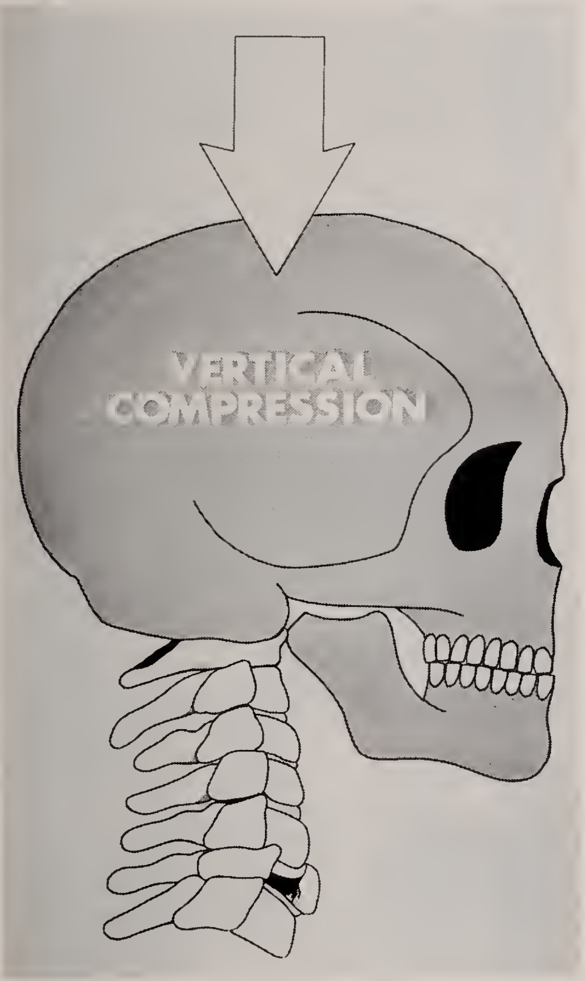


Fig. 5—Vertical compression injuries result in a bursting injury of the vertebral body, where the body above has compressed the body below and produced bony displacement posteriorly into the spinal canal.

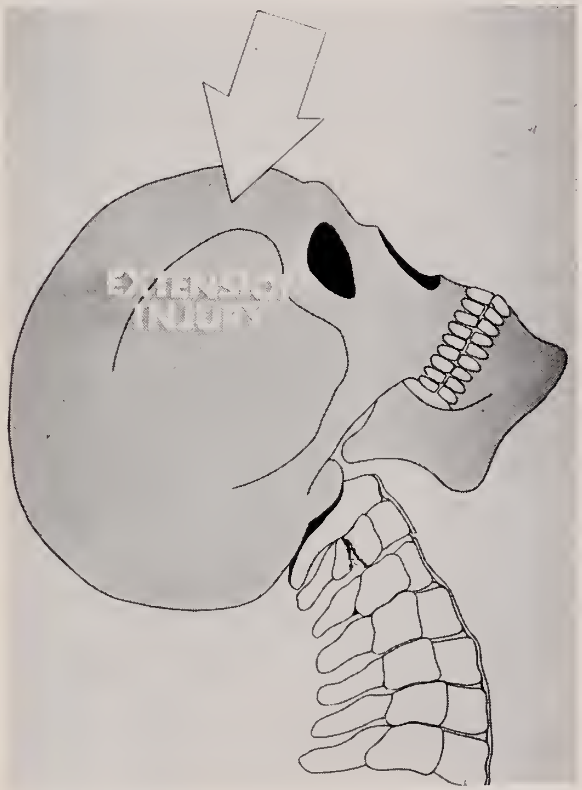


Fig. 6—Extension injuries produce fractures in the posterior elements of the neural complex and are usually associated with disruption of the anterior longitudinal ligament or avulsion fractures of the anterior bodies. The most common injury seen with this mechanism is a fracture through the neural arch of the second cervical vertebra.

dislocations that were reduced to be stable. 100% of the extension injuries to be stable, and 80% of anterior subluxations to be stable. The displaced flexion compression injuries with wide separation of the posterior elements were excluded from this study, since those were treated surgically at the beginning.

Thoracic and Lumbar Spine

Injuries to the thoracic and lumbar spine may be categorized accordingly (Table): those involving angular stress to the thoracic and lumbar spine, which would include flexion-extension, lateral bend, and rotation, and those involving non-angular stress to the thoracic-lumbar spine, which would include distraction-compression, anterior and posterior shear, and lateral shear.

TABLE
Classification of Spinal Injuries

Cervical	Thoracic/Lumbar	
Flexion-Compression	Flexion-Extension	Angular Stress
Flexion-Rotation	Lateral Bending	
Compression	Rotation	
Extension		
	Anterior/Posterior Translation	Non-Angular Stress
	Lateral Translation	
	Distraction/Compression	

Flexion-Extension Stress

Flexion injuries are the most common of all injuries involving the thoracic and lumbar spine. They most frequently occur at the thoracolumbar junction and are rarely associated with neurologic damage. Severe comminution of bony cortex, however, may compromise the neural canal and result in neurologic squelae. This is most uncommon. The flexion axis of the spine is close to the center of the intervertebral disc. Consequently, the compressive forces on the anterior part of the vertebral body are up to 4X the tensile forces on the spinous processes or supraspinal ligaments.[10] With hyperflexion stress, the vertebral body will undergo failure anteriorly, producing a wedge-shaped fracture alone, leaving the posterior cortex minimally disturbed. For the most part, these injuries are considered stable and will never produce acute instability, since the posterior ligament complex and posterior column is intact. Multiple compression fractures over contiguous segments, however, may result in chronic instability with delayed but progressive angular deformity. Hyperextension, although common in the cervical spine, is quite rare in the lumbar and thoracic spine. Occasionally, an avulsion fracture of the anterior lip of the vertebral body or a fracture through the pars interarticularis may develop from hyperextension. Neurologic damage is, again, rare.

Lateral Bending Stress

Angular stress in lateral bending may result in a failure of the vertebral body and a portion of the lateral mass. This presents as a lateral wedge fracture similar to a hyperflexion, anterior wedge fracture. Again, this is a stable injury and is rarely associated with a neurologic deficit.

Rotation Stress

Rotational stress past the physiologic range may produce a fracture with dislocation of the vertebral body (Figures 7 A/B). Anatomically, the arrangement of the facets in the lumbar spine prevents rotation, while in the thoracic spine, rotation is comparatively free. The abrupt transition at the thoracolumbar junction makes this region more susceptible to rotational stress. Injuries due to pure rotation are extremely rare, whereas a combination of flexion and rotation is the most common cause of fracture-dislocation of the thoraco-lumbar spine. This is classified also as the "slice fracture" by Holdsworth.[8]

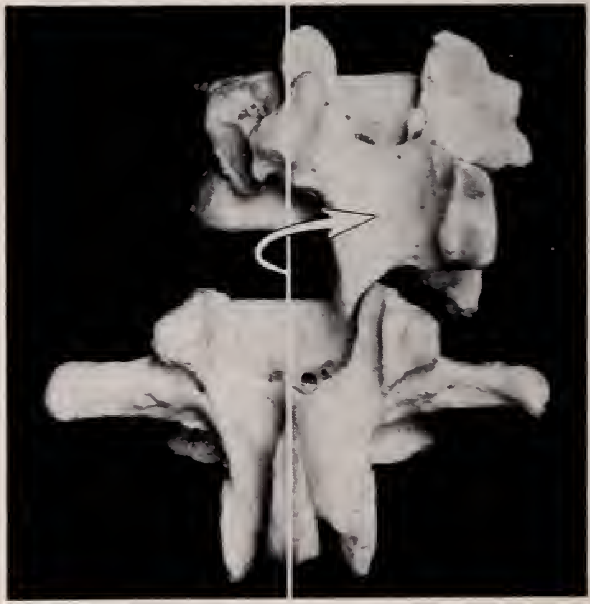


Fig. 7A—Rotational stress (7A) combined with flexion may lead to a fracture dislocation or the so-called "slice fracture."

Since a disruption of both anterior and posterior columns has occurred, the effect is a transverse translational displacement. This is one of the most acutely unstable of all spine injuries and a neurologic deficit may be expected in 70 percent of these injuries.

Compression-Distraction

Compression stress leading to fracture results from pure vertical loading without flexion, rotation, or lateral bend.[13] This is often confused with the anterior wedge of flexion injury, but in contra-distinction to the wedge injury, the compression injury involves the whole vertebral body. Severe compression loads produce the burst-type fracture (Figure 5), well described by Holdsworth.[8] These injuries are acutely stable, but may demonstrate chronic instability. Neurologic damage is possible and results from displacement of bony fragments posteriorly. Distraction or ten-

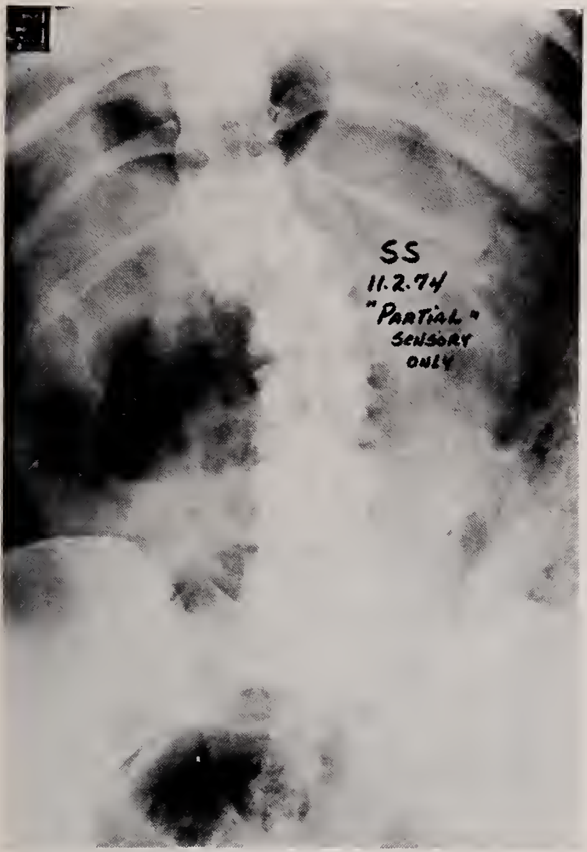
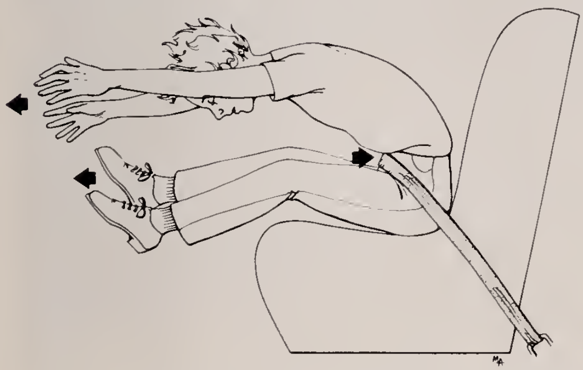
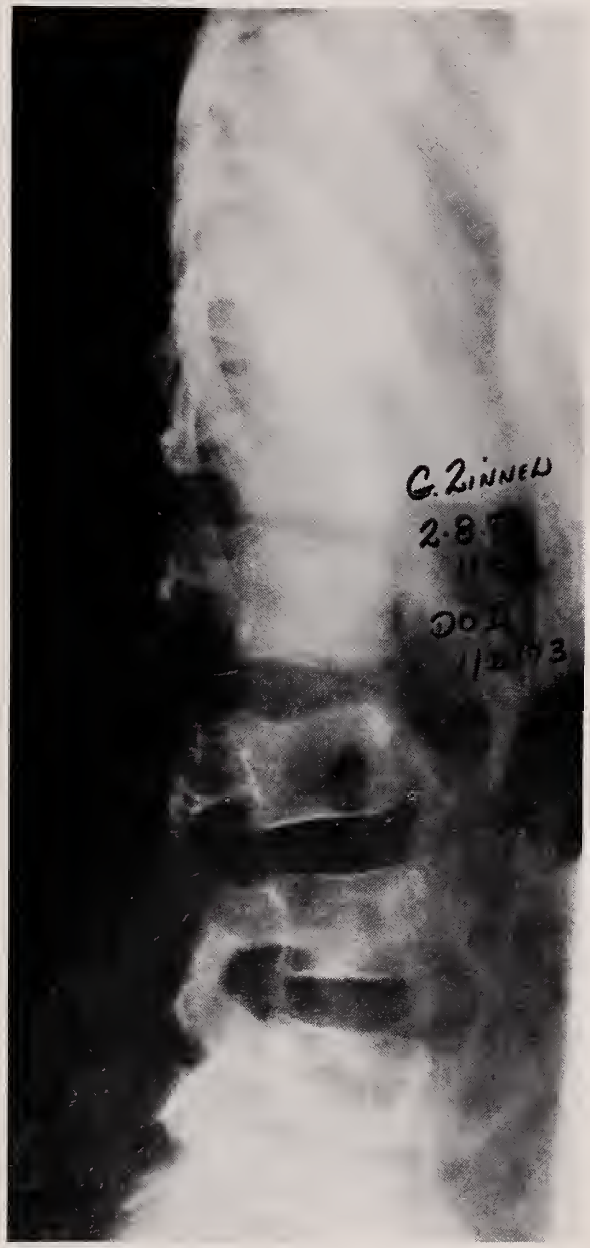


Fig. 7B. This is, in effect, similar to transverse translation displacement and is the most acutely unstable of all spine injuries.





Figs 8A/B—A distraction or tension fracture should not be confused with the pure flexion injury. This tension fracture is often associated with seat belt injuries and may result in disruption of both structural columns, through soft bone, through soft tissue (8B-right), or a combination of both.

sion fractures are not common, but are usually seen in patients who were wearing a lap seat belt at the time of injury (Figures 8 A/B). The distraction or tensile force may result in disruption of the spine continuity, either through bone, through soft tissue support, or a combination of both. The pure distraction fracture through bone (Chance Fracture)[2] appears the more stable variety, perhaps because of the interdigitation of fracture surfaces. However, since both structural columns of the spine may be damaged, acute instability is possible. Neurologic damage occurs in these injuries in approximately five percent of patients.

Shear

Translational displacement of the spine may occur in the anterior-posterior or lateral planes. Since these injuries damage both structural columns, acute instability is present. In the thoracic spine, some authors have felt that soft tissue and rib support will prevent progressive deformity.[8] That has not been our experience, and we have found these injuries, along with the flexion-rotation injury (which also results in transverse translation) (Figure 7B), to be the most unstable of all injuries. Neurologic damage is common.

Treatment

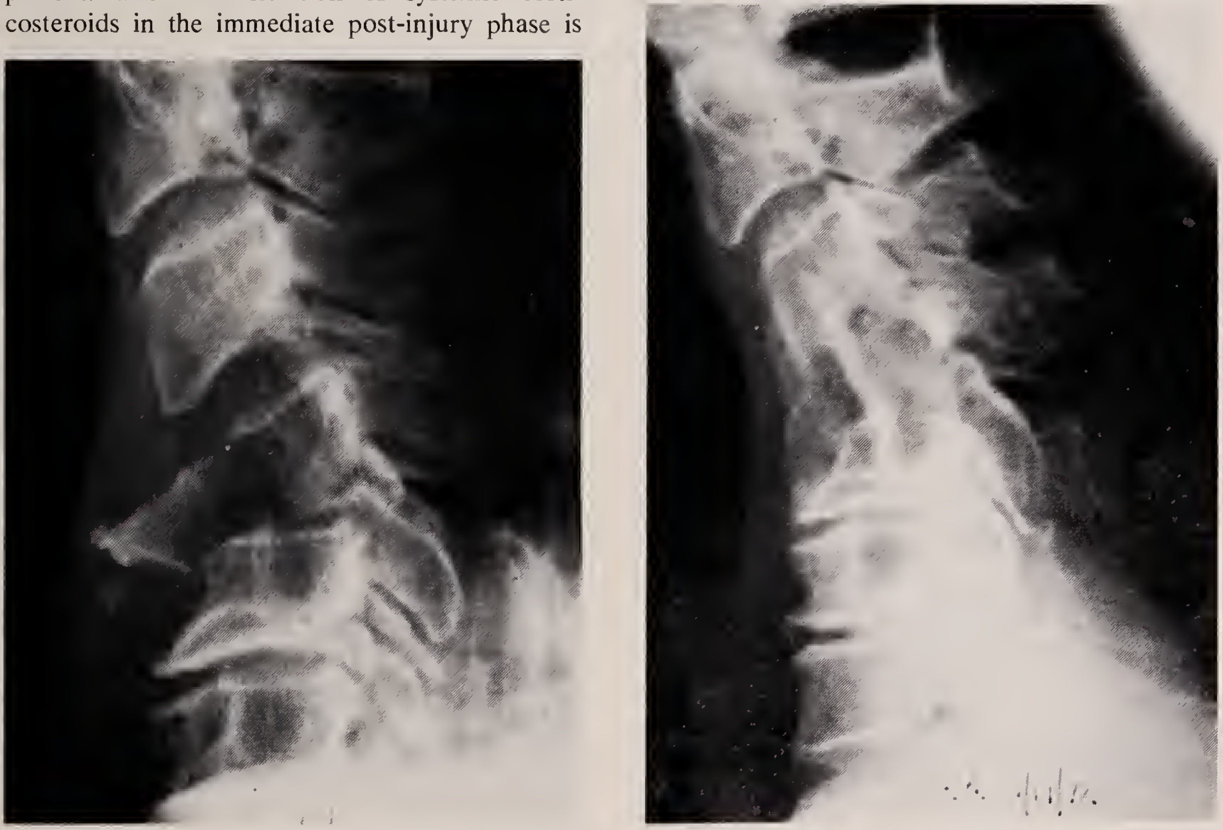
Treatment of the damaged spine should be directed toward preserving neurologic function and improving it when possible, stabilizing unstable injuries, and restoring anatomical alignment. The approach that one should take would be based on the presence or absence of spine stability.

Treatment of Cervical Spine Injuries

Those patients with a *stable injury without neurologic deficit* need only to be protected until their symptoms have subsided. Such injuries would include a minimal compression fracture without disruption of the posterior soft tissues. These patients occasionally need to be hospitalized for a few days for observation and application of a cervical spine brace or a soft collar. A period of six to eight weeks of immobilization allows for soft tissue and bony healing. *Stable injuries with neurologic deficit,* be it nerve root or cord, should be carefully evaluated and protected to prevent further neurologic damage. In this situation, the treating physician must be wary of a multiple level injury where an unstable fracture or dislocation might masquerade as a stable one. This question can be resolved by careful flexion and extension Xrays within the first 48 to 72 hours. The most classical injury producing a neurologic deficit and a stable skeletal lesion is the vertical compression fracture (Figure 5), where posterior impingement on the spinal canal occurs as a result of displacement of bone and disc material. The institution of skeletal traction through the skull is usually indicated to protect the cervical spinal cord from further damage, to maintain alignment of the cervical spinal canal, and to decrease posterior bony impingement on the spinal cord. Careful neurological monitoring of these patients is essential. They should be treated in the same fashion as those patients with unstable injuries and neurologic deficits to be discussed in the subsequent paragraph.

Unstable cervical spine injuries manifest by rotational or translational malalignment are best managed initially with skeletal traction. Realignment of the spinal canal is the first step in converting an unstable injury to a stable one. We begin with 15 to 20 pounds of traction, depending upon the level of injury, using more weight for the lower cervical spine injuries. The patient is carefully monitored with lateral cervical spine Xrays, in order to assess alignment of the spinal canal. Appropriate adjustments in the direction and weight of traction are made until the malalignment is corrected. This principle applies to patients with or without a neurologic deficit. Traction provides excellent protection for the neurologic tissues and allows most displacements to be rapidly reduced. In the *unstable skeletal injury without neurologic deficit,* we prefer the use of a halo for traction. After alignment of the spinal canal is restored and symptoms have subsided, the application of a body cast and incorporation of the halo device to the cast allows early ambulation and discharge from the hospital. The halo-body device is continued for a period of 12 to 16 weeks. In fractures with a high incidence of late instability, such as flexion-compression injuries with disrupted posterior elements, or anterior subluxations (20% late instability after conservative treatment), surgical intervention may be elected for bony stabilization. This should not be attempted prior to a period of stabilization in traction in order to avoid further damage to the neurologic tissues and to allow the acute edema around the spinal cord and nerve roots to subside.

In the *unstable cervical spine injury with neurologic deficit,* a thorough neurologic examination must be performed in order to rationally treat the patient. This means testing always for sacral sparing (anal sphincter tone and perianal sensation). A complete cord injury is defined as a total absence for 24 hours of motor and sensory function distal to the level of injury. A complete cord injury also implies no hope of neurologic return, regardless of the method of treatment. When a documented complete lesion is present, the most that can be achieved by treatment is to protect the cord above the lesion and, hopefully, salvage an additional root. In contrast, the incomplete cord lesion must be carefully protected from further damage. One may anticipate a partial if not complete return of neurologic function depending upon the type of neurologic injury present. The administration of systemic corticosteroids in the immediate post-injury phase is generally accepted as an adjunctive measure to prevent further cord damage in these patients. However, realignment of the spinal canal remains the mainstay of treatment, and is the most effective means of relieving pressure on the neural tissue. The only indication for emergency surgical intervention in a cervical spine injury is the presence of a documented progressive neurologic deficit after the spinal canal has been aligned by traction. This situation is extremely rare and most patients may be stabilized in traction for a period of seven to 10 days without endangering their neurologic function. In contrast, early surgical intervention, either anteriorly or posteriorly, may be associated with significant mortality.[14,15] In the complete cord lesion, the use of the halo body cast is contra-indicated, because of the absence of protective sensation below the level of injury. In those cases where anterior interbody fusion can provide early stabilization, rehabilitation is expedited. When a partial cord lesion is present and the injury is reduced in traction, neurologic return usually occurs. If the



Figs. 9A/B—This flexion-compression fracture resulted in an incomplete cord lesion. The injury was partially reduced in traction and some improvement in neurologic function resulted. An anterior decompression was elected because of persistent neurologic deficit (partial) and bony impingement on the cord. This was followed with an anterior fusion (9B-right) Complete recovery with spinal stability was achieved.

neurologic level plateaus and full recovery no longer appears possible, a myelogram should be done to rule out extrinsic pressure on the cord. A myelographic block in the presence of anatomic spinal alignment would suggest a ruptured intervertebral disc. Decompression of the neural elements should be carried out. If the myelogram is normal, the incomplete lesion should be managed on the basis of the spinal fracture and its propensity for instability. Most of these patients may be treated by the application of a halo body cast or a halo vest. This will allow early mobilization and rehabilitation of these patients without adding surgical trauma that might jeopardize neurologic function of the spinal cord.

Should a surgical decompression or stabilization be elected, the operative surgeon has the choice of an anterior or posterior approach. Below the level of C3, anterior interbody fusion will provide excellent stability. It also provides a means of direct decompression of the anterior spinal canal where most bony compression and disc protrusion occurs (Figures 9 A/B). However, when a facet joint is locked and cannot be reduced in traction, it is best approached posteriorly. The locked facet may be visualized directly and reduction usually obtained with minimal difficulty. This should be supplemented by a posterior bony fusion. External immobilization with a cervical brace is usually required for from 12 to 16 weeks following either anterior or posterior fusion. Laminectomy is indicated only for removal of foreign bodies or bony fragments protruding into the canal, as commonly seen with gunshot wounds.

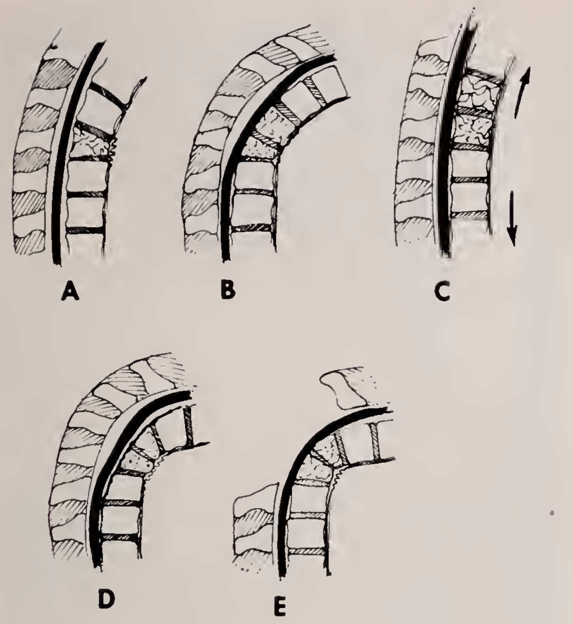
Injuries to the atlanto-axial complex must be considered separately in treatment as in classification. Bursting fractures of the ring of C1 (Jefferson's Fracture) are intrinsically stable and require protection only for the immediate post injury period. Injuries to the transverse ligament of C1 have been studied by Fielding and coworkers.[4] They showed that when x-ray evidence of anterior displacement of more than five mm. occurs between the anterior ring of C1 and the odontoid, there is a complete tear of the transverse ligament. This is an unstable injury and should be surgically fused. Posterior surgical fusion from C1 to C2 is the approach of choice. However, these patients must be maintained in some external fixation device such as a halo body cast post surgery. Odontoid fractures have received a variety of treatment in the past, with many authors favoring surgical intervention and others condemning it. Recent experience with the management of odontoid fractures has shown that by reduction of the fracture using a halo for traction and subsequent immobilizations in a halo body cast for 16 weeks, 95% of these injuries can be expected to heal without surgery.[12]

Thoracic/Lumbar Spine

Stable injuries to the thoracic and lumbar spine without neurologic deficit require little treatment. This group of injuries would encompass anterior wedge, lateral wedge, and burst (compression) fractures. Analgesics for pain, along with bed rest for several days, is usually sufficient. Transient ileus is common and should be treated when present.

The use of a brace or body jacket for one to two months may offer some benefit. We favor the Williams chair back brace for lower lumbar spine injuries and the Jewett brace for injuries involving T8 to L2. Injuries higher than T8 would require an over-the-shoulder plaster body jacket. There is little evidence that these supports appreciably affect the end result; however, they do little harm and patients often seem more comfortable with their use. The follow-up from such injuries demonstrated that 25% of patients are asymptomatic, 55% have mild discomfort, and 20% have enough symptoms to produce some disability.[10]

Stable injuries with neurologic deficit require a careful but realistic approach. Those lesions associated with complete and persistent interruption of spinal cord function over 24 hours will not be benefited by surgery directed at reversing the neurologic deficit. Treatment, rather, should be directed toward the patient's rehabilitation as a paraplegic.[6] No longer is it justified to perform a laminectomy "in order to assure the family and patient that everything possible was done." Not only is this approach without documented benefit, but the laminectomy may produce spinal instability, converting a stable injury into an unstable one (Figure 10). It is our feeling that maximal neurologic damage occurs at the time of injury and heroic measures such as cord cooling and myelotomy offer little. On the other hand, incomplete cord lesions or lesions involving the cauda equina

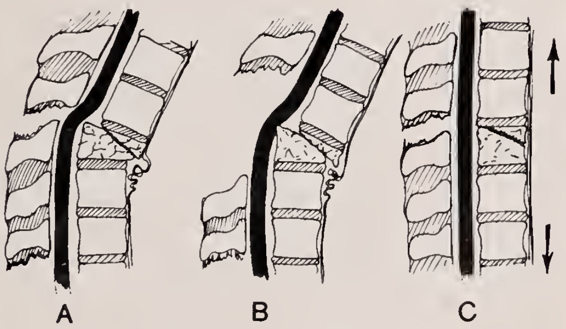


Figs. 10A/B—A single compression fracture is a stable injury and is not associated with neurologic deficit (10A). Multiple compression fractures may result in excessive spinal angulation and lead to neurologic deficit (10B). Anatomical realignment (10C) or anterior decompression (10D) can relieve the pressure on the cord. Laminectomy does not decompress, but results in greater instability and deformity with increased pressure on the cord (10E).

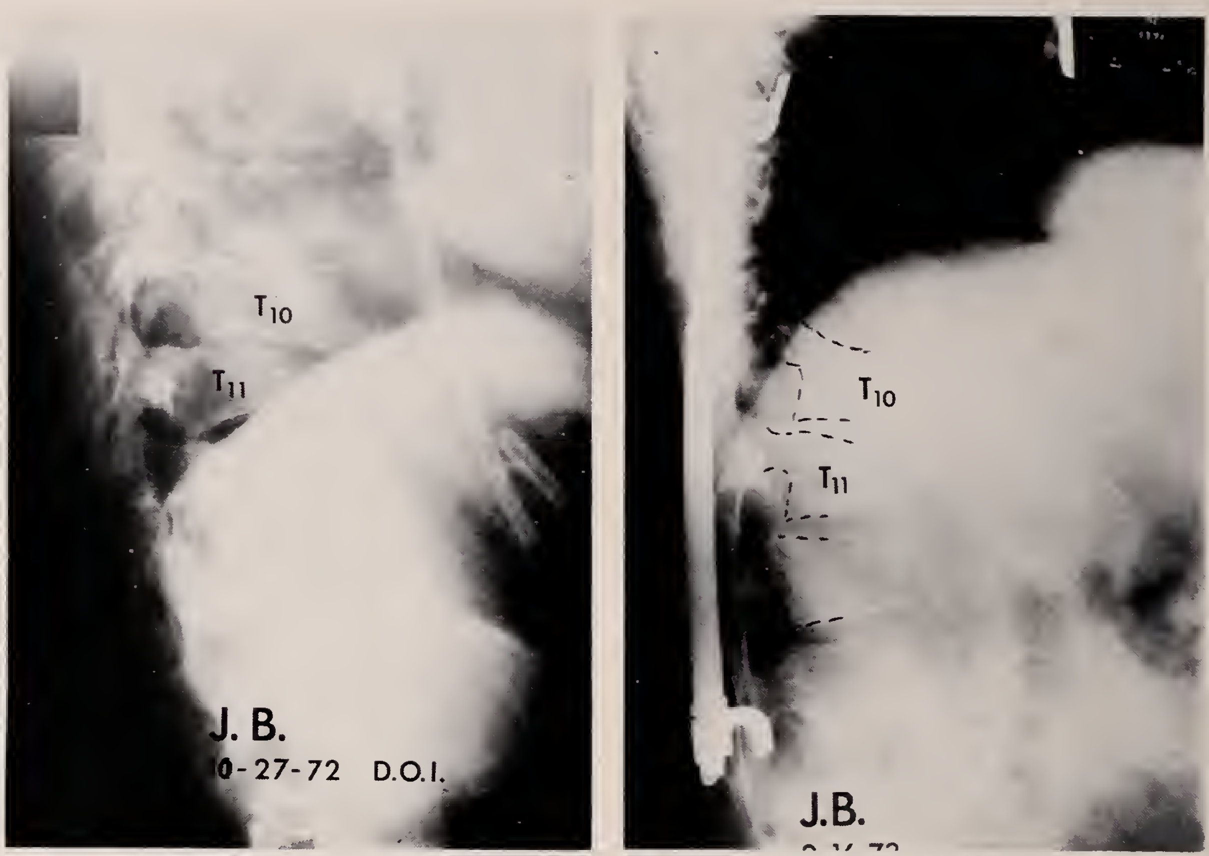
may result in significant functional neurologic improvement, provided the bony impingement is removed. Laminectomy as an isolated procedure rarely, if ever, adequately decompresses the neural elements. The compression that exists with these injuries is anterior and, therefore, posterior "unroofing" procedures do little more than produce spinal instability.[1] Anatomical reduction of the fracture is, in our minds, the most efficacious and beneficial method of achieving decompression (Figure 10). On the other hand, a limited laminectomy over a single level carried out at the time of fracture reduction has proven a useful procedure in identifying and removing loose bony fragments and disc material within the canal. It is also helpful in visualizing the dura as the fracture is being reduced and realigned by the Harrington device. Through this limited opening, one may palpate the anterior "step-off" prior to fracture reduction and after spinal realignment to assure that decompression is complete and thorough.[5]

For incomplete stable lesions involving the thoracic spine where treatment has been delayed for more than two weeks, we have favored a transthoracic anterior cord decompression followed by an anterior fusion, using rib or iliac bone as a strut graft. If stability has been jeopardized by this approach, a posterior spine fusion with Harrington rod instrumentation is carried out two weeks later. Incomplete lesions involving the cauda equina are decompressed through a posterior-lateral approach, removing the facet joint on one side at one level, allowing access to the bony fragments pushing on the dura anteriorly. These can then be removed without undue traction on the dura. The spine must be stabilized internally and a fusion carried out, since instability is produced by this approach. Incomplete cord or cauda lesions should be approached with optimism, since significant neurologic recovery may result with adequate anterior decompression.

Unstable thoracic and lumbar spine injuries without neurologic deficit should be managed by open reduction of the fracture, internal fixation, and spine fusion. Untreated, these injuries may further displace, resulting in neurologic damage, increased instability, progressive deformity, and disabling back pain. Closed reduction alone of these fractures may lead to neurologic damage.[10] Likewise, we have found closed methods usually ineffective in maintaining reduction and preventing progressive deformity. For the operative approach to be most effective, it is best performed within one week of injury, before consolidation of the hematoma and granulation of tissue occurs. Prior to surgery, the patient should be managed on a Foster or horizontal Stryker turning frame.



Figs. 11A,B,C—Unstable injuries with or without neurologic deficit must be stabilized to prevent late deformity and pain. Laminectomy alone does not decompress, but will lead to greater deformity (11B). Anatomical realignment is the preferred method for decompressing the neural elements (11C).



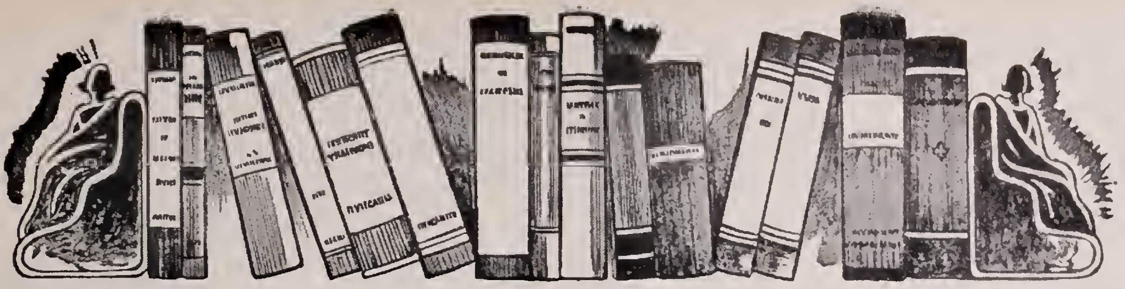
Figs. 12A (left) & 12B (right)—This twenty-eight year old male sustained an enterior-translational dislocation at T10-11, with a partial cord lesion. He underwent a posterior-lateral decompression and reduction with Harrington instrumentation of the fracture. He has obtained full neurologic recovery with a stable, painless spine.

A vertical turning circle-electric bed should not be used, since axial loading of the spine may result in severe displacement of the bony fragments. Patients are ambulated within one week of surgery, after the application of a body cast. The case immobilization is continued for six to eight months, until the bone fusion is solid.

Unstable injuries with neurologic deficit require attention to the farcture as well as to the neurologic status of the patient. The unstable fracture should be stabilized to prevent late deformity, skin ulceration, and pain. Anatomical realignment of the fracture remains the most certain method of decompressing the neural elements (Figure 11). In fractures associated with incomplete cord lesions or fractures involving the cauda, a limited laminectomy, carried out in conjunction with the fracture alignment and internal fixation, can assure removal of loose bony fragments and disc material, and facilitate inspection for adequacy of reducton (Figures 12 A/B). For incomplete, unstable lesions, especially in the thoracic spine where treatment has been delayed for more than three to four weeks, complete reduction of the fracture may not be possible by the posterior approach. In these cases, we would favor anterior cord decompression and anterior spine fusion through a transthoracic approach.

The post-operative management depends on the strength of fixation and the presence of sensation. If the fixation is secure (we have found the Harrington distraction device superior in this regard), and sensation intact, a plaster cast is applied and the patient begun on rehabilitation within one week. If sensation is absent, a brace or bi-valved polypropylene body jacket is substituted for plaster. Bracing for three to four months is usually adequate.

References will be found on page 701.



Book Reviews

ATLAS OF VASCULAR SURGERY, Third Edition. Falls B. Hershey, M.D., F.A.C.S. and Carl H. Calman, M.D., F.A.C.S. The C. V. Mosby Company, 1973. Price: $35.00.

This is a welcomed edition of a commonly used reference of vascular surgeons. The previous editions were in 1963 and 1967. This volume almost doubles the number of pages of the second edition. Several new chapters have been added to it. There are 681 illustrations in the third edition and 504 pages. All of the valuable material of the second edition is retained and supplemented by new chapters on the following subjects: Operations on the Common Femoral and Profunda Femoris Arteries; Other Bypass Operations to the Groin; The Upper Extremity, Superior Mediastinum, and Thoracic Outlet; Surgical Prevention of Pulmonary Embolism.

Part of the original chapters of the second edition, however, have been retained and have been significantly amplified by additional illustrations, photographs, and by selective references. Some of the latest technical advances have been emphasized which include surgery on the profunda femoral artery as well as the use of the Mobin-Uddin caval filter for inferior vena cava interruption.

In summary, the *Atlas of Vascular Surgery,* Third Edition, gathers together in one book diagnostic and therapeutic material required by the vascular surgeon in applying his skills in all of the common and most of the uncommon problems in vascular surgery today. Only some of the most recent and narrowly applied techniques in management of portal hypertension and its complications are not included. Not only is this book a must for practicing vascular surgeons but for the general surgeon as well.

Paul G. Gannon, M.D.
Minneapolis, Minnesota

A HANDBOOK OF HUMAN SERVICE ORGANIZATIONS by Demone, Harold W., Jr., and Harshbarger, Dwight. Behavioral Publications, New York, New York, 1974, 600 pages, Price: $19.95.

This is one of the best books I have ever read. Unfortunately, the title is so misleading that if I didn't have to review it I would never have opened it.

I expected to find a dry collection of data on social services but instead, the very first line of the book sets a different tone—it reads: "Do-gooding is a major growth industry." From the very first page I was hooked by a book that is harder to put down than "The Exorcist" and much more descriptive of today's demonology.

I can particularly recommend this book to the readers of MINNESOTA MEDICINE because the authors chose . . . "The perspective of organizations attempting to remain viable and constructive in an increasing complex, turbulent, technological, and depersonalized society."

The book was designed for administrators and students in management, but the concise discussion of organizations that serve social needs is particularly relevant in medicine today.

This series of readings is so well edited that it is hard to select a favorite section from the 600 pages but the chapter entitled "The Health Syndicate: Washington's Nobel Conspirators" written by Elizabeth Drew is by itself worth the price of the book.

John B. O'Leary, M.D.
Minneapolis, Minnesota

THE LOW BLOOD SUGAR COOKBOOK, Blevin and Ginder, Doubleday and Company, 1973 520 pages and price: $8.95.

As a former Editor of MINNESOTA MEDICINE I used to maintain that a member of the Board of Editors should, on occasion, be able to edit as well as review topics outside of his chosen specialty.

I qualify as a breast surgeon, but as an Emeritus Editor, I presume I should now swallow my own words and review the cookbook that was sent to me.

This book did not provide any symptoms of hypoglycemia, nor under the circumstances should it have, though it might have mentioned for the individual with an occasional hypoglycemia that the symptoms may include sweating, shakiness, trembling, tachycardia, anxiety, nervousness, weakness, fatigue, hunger, nausea and vomiting. With any of these symptoms the patient should consult her own physician for an accurate diagnosis, as there could be serious, underlying disease.

The diets and some of the recipes are intriguing. For an individual who speaks of the need for a snack because of her "low blood sugar," many of the recipes might satisfy her. Their low caloric value would be of additional value in controlling the weight-gaining quality of between-meal snacks.

Perhaps because of my occasional uncontrollable urge to stop with one piece of candy, I was intrigued by some of the candy recipes, which were made in the blender, spread out on the pan, cut into pieces and not cooked. The ability to make raisins out of apples and currants out of plums was novel and might be worth trying to see if that would satisfy my occasional candy urge.

I found the index adequate, and the recipes for a variety of dishes were not lost for lack of indexing. This item lends value to all books, but it is absolutely essential in a reference book of this character.

This book should make an excellent addition in a doctor's library, in order that he might provide for some of his patients an appetizing hypoglycemic diet. It should be of untold value on the kitchen shelf for the hypoglycemic patient.

Carl O. Rice, M.D., Ph.D.
Editor-Emeritus

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(Continued on page 732.)

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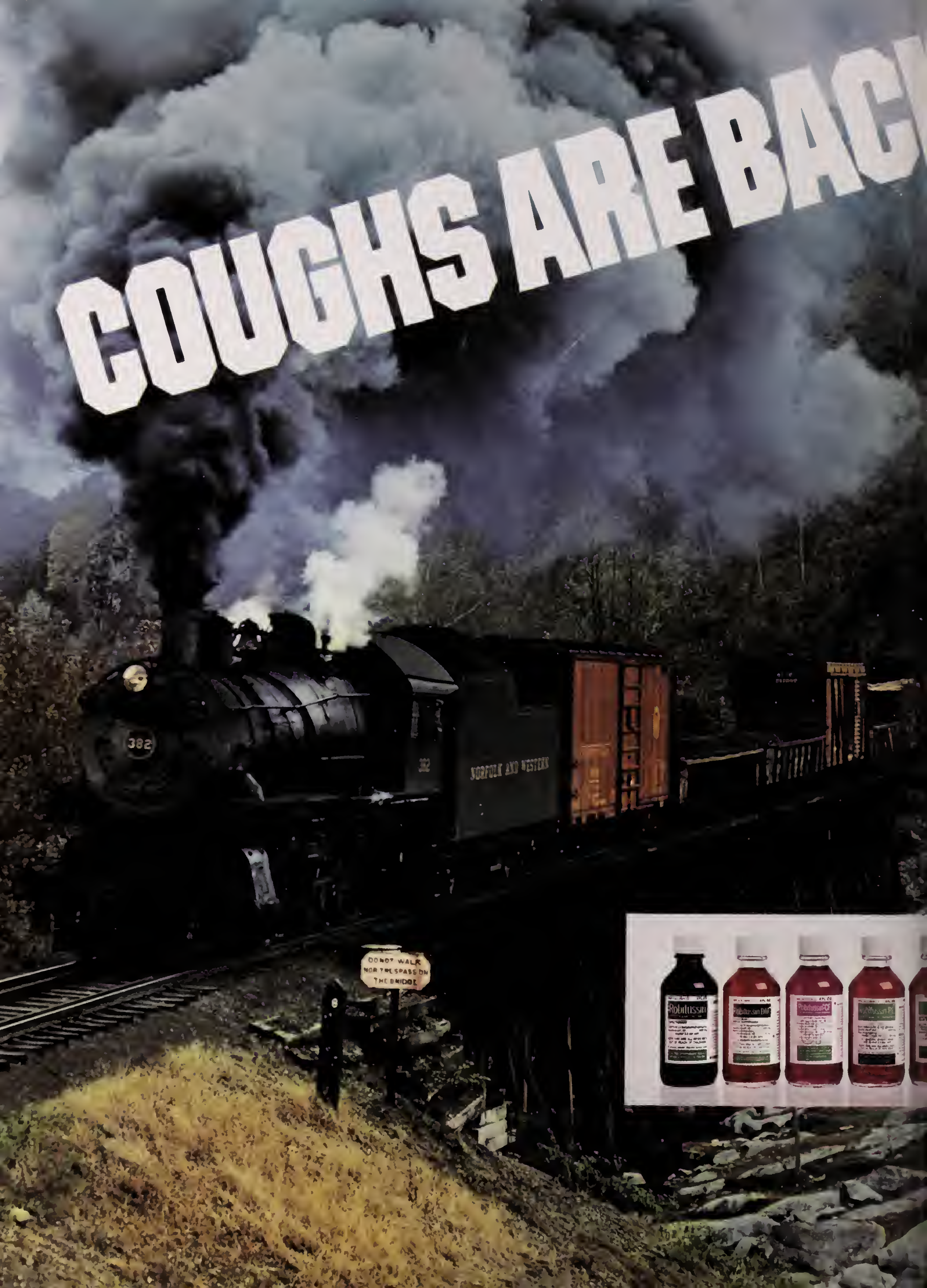
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Section 44. Minnesota Statutes 1974, Section 147.23 is amended to read:

147.23 (HOSPITAL MEDICAL STAFF, MEMBERSHIP) Nothing contained in Laws 1963, Chapter 45, shall be deemed to grant to any person the right to be admitted to the medical staff of any hospital. *If a hospital withdraws the right of a person to practice medicine or osteopathy at that hospital, or limits the surgical procedures he may perform within that hospital while retaining the physician on their staff, the hospital shall promptly inform the board of this action. When the board receives a report pursuant to this section they shall treat it in the same manner as prescribed for receipt of complaints in section 5, subdivision 1, of this act.*

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Medical Care for an Aging Population
Implications for Medical Education*

WINSTON R. MILLER, M.D.†

With an aging population medical care needs are shifting to preventive maintenance for maximum health-years of normal living. Medicine must provide and teach comprehensive geriatric care.

"WE LIVE IN A nation where acute disease is no longer the main health problem. The chief need for a physician is no longer to stave off death but to help his patient face the physical and emotional buffeting of life. His goal should be to maintain health through disease prevention or, at least to contain chronic disease so that the patients can live a normal life."[1] James, has defined four stages of medical care as follows: "(1) Prevention, (2) Early detection, (3) Care of Acute Illness, (4) Rehabilitation or long term care. To most graduates of our medical schools, stages 1, 2, and 4 seem dull. There is little excitement in rehabilitation and care of chronic disease between crises, while prevention and early detection lack the intellectual stimulus of crisis care. But the need for total care is here. It cannot be ignored because it is uninteresting."[2]

The glorious era of crisis medicine with renowned accomplishment in prevention and cure of infectious disease and the development of superspecialization has run its course. This period described as the "Era of Pasteur" ended in 1954 when the death rate in this country reached its all time low. That year we entered the "Era of Darwin and Freud" "marking the point when our main health problems became congenital and prenatal defects, degenerative diseases, mental illness and conditions produced by our environment . . ." "These are new foes that hospitals, physicians, scientists and educators, geared to fight an earlier war, are ill prepared to face." Medicine is "caught in the point of impact between two revolutions."[1]

This point of impact is expressed succinctly: "When national political leaders are compelled to highlight the failure of medical performance in long-term care of the chronically ill and aged, the time for the community of physicians to provide leadership in this field must be overdue."[3] The most rational solution for this need for leadership is expansion of the emerging broad specialty referred to as Gerontology or Geriatrics. Social, political, economic, ethical and medical forces may combine to accelerate the development and status of this specialty. A dedicated patient care trustee is needed to serve as the patient's personal advocate. If physicians abdicate this responsibility, some other patient care manager will take over the responsibility and corresponding authority.

This paper will describe the needs for this specialty as they exist and as futuristic research indicates will increase during the next 25 years. To begin with an historically proven premise often forgotten: "Medicine is a service profession which responds to the needs and desires of the society it serves." Institutions for medical education also respond to society's needs and desires but more specifically they respond to the particular interests of the profession as a whole. As the specialty of Gerontology and Geriatrics develops in response to social forces, this group of specialists will stimulate educational programs in Gerontology and Geriatrics in the Schools of Medicine. In Great Britain the specialty developed as a direct result of government building of Geriatric Day Care Hospitals. Teaching programs in the medical schools followed. In Minnesota, the movement has just started with appointment of a Medical Director in at least 225 of the 246 Skilled Nursing Facilities responding positively to the recommendation made by the AMA and mandated by Federal Regulations. The State Medical Association has co-sponsored and sponsored several training seminars for these physicians who will function as Geriatricians.

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*Presented at Continuing Medical Education Program "Human Aging II," University of Minnesota School of Medicine, April 10, 1976.

†Clinical Assistant Professor, Internal Medicine, University of Minnesota School of Medicine; Director, Section on Quality Assurance and Review, Division of Health Facilities, Minnesota Department of Health, 717 Delaware Street S.E., Minneapolis, Minnesota.

Gerontology and Geriatrics are derived from the Greek word "geras," meaning "old man." Gerontology would then mean the science of old men and Geriatrics would mean the practice related to old men. Strictly speaking, therefore, the specialty relates specifically to the aged. However, since the principal problems of the aged are chronic illness, the specialty would include chronically ill persons requiring long term care. Perusal of the literature on Gerontology and Geriatrics reveals an expanding body of fundamental and applied science and art in the problems of aging. Like Primary Medical Care, of which Geriatrics should be considered a part, holistic performance of optimum patient care requires more than partial contributions by each of the multitude of existing medical specialists.

Population to be Served

The number of persons 65 years of age or over has almost doubled since 1930. Projections for the year 2000 indicate a further population increase of at least 22%[4] At the same time the school age population, which is the other group with heavy utilization of health care services, will decrease by the same percentage. These calculations are based on current fertility and death rates. Should both of these rates drop further in the next 25 years, as some have predicted, the growth of the geriatric population may go as high as 62%.[5] Health care service needs and demands are therefore shifting significantly from the young to the elderly.

Socio-economic changes have increased the relative affluence of older Americans and promoted earlier retirement. Retirement incomes are being increased by public support of private initiative and by cost-of-living increases in Social Security. There is evidence that earlier retirement has already started: in 1974 only 81% of 55-64 year old men were in the active work force.[5] Research workers indicate these trends will continue and the average retirement age by the year 2000 is optimistically estimated to be 55. They describe an active, independent and influential retired population subgroup, age 55-74, called the "Young-Old."[5] This subgroup can be expected to articulate its needs and desires in society, and current indicators suggest greater emphasis on the quality of life and individual choices in life styles.[5] A strong movement of Quality Assurance has already started, placing emphasis on the quality rather than the quantity of health care services in particular and of life in general. Organizations such as the Institute for Society, Ethics and the Life Sciences are leading society to focus on "How well we live" rather than "How long we live."[6] The challenge to health care professionals is to change the emphasis from episodic crisis care to continuing maintenance of maximum capability for normal living.

The "Old-Old" subgroup (75 and over) is expected to show the greatest proportional increase in the next 25 years. Although this age group is generally thought to be totally dependent, less than 10% of them are now in Nursing or Boarding Care Homes and only 15% are homebound. Thus 75% are maintaining a more or less normal life style today. If the current therapeutic nihilism can be corrected, further improvements in functional independence may be expected. As one author stated: "Older fragile persons can remain in the community as long as proper supports are available."[7]

Another population subgroup has great importance from the standpoint of Gerontology. This group, the Old-Young, ages 40-54, experience sub-clinical or early clinical manifestations of degenerative chronic disease. Both primary and secondary prevention concepts of degenerative disease play a large part in optimum medical care for this subgroup. Many research workers and personal physicians have already adopted the continuing maintenance philosophy for this subgroup, but they frequently drop it at age 65, particularly if patients are admitted to long term care facilities.

In 1974 people age 45 and over received 56% of all days of hospitalization and 37% of all physician visits.[8] These percentages can be expected to increase significantly as our society moves from its past emphasis on youth and economic growth to the new realities of a balanced population and its needs for sustaining economic stability, Society's needs and desires for health care services can be expected to change toward maintenance of physical and psychological independence.

Institutional Patterns

From the beginning of this country and into the 20th Century the most prestigious hospitals followed the precedent in Great Britain and limited their services to acute and curable illnesses.[1] The incurables and chronically ill were excluded. Asylums, State Hospitals, Poor Farms, Custodial Homes for the Aged and Domiciliaries housed those who could not manage on their own. Medical education and practice focused on acute illnesses. The chronically ill and aged were largely ignored. From 1900 to 1951 the confused elderly were admitted to State Mental Institutions in increasing numbers and large geriatric wards were developed. Institutions for the chronically ill, aged and poverty stricken, conditions which went hand-in-hand, constituted little more than custodial warehouses. Health care professionals including physicians, paid little attention to their care or the characteristics of their illnesses. Remnants of these conditions and attitudes persist in many of the Long Term Care Facilities today.

Nursing Homes developed as a purely American phenomenon after passage of the Social Security Act of 1935. Residents of public long term care institutions for the chronically ill and aged were initially excluded from Social Security and welfare support, but a voluntary hospital lobby succeeded in removing the exclusion from private institutions. "At one stroke, completely without plan or intention, the nursing home system was born."[1] Furthermore the payment system promoted proprietary Nursing Homes by paying them more than Nursing Homes supported by local taxation or private philanthropy. A further big change came with the passage of Social Security Amendments in 1965 initiating Medicare and Medicaid and accompanying steady streams of federal regulations for control of hospitals and long term care facilities. The Medicare-Medicaid Act with its social concept of optimum health care as a human right has had profound effects on the health care system in this country.

Nursing and Boarding Care Homes have increased rapidly in both numbers and size. Social acceptance and financial support, both private and public, have stimulated construction of modern long term care facilities with designs which seem to be a cross between a hospital and a modern hotel. Eighty-five percent of long term care facilities in this country are proprietary (only 40% in Minnesota) and proprietary operation has proved to be financially rewarding. During the 35 year period of rapid expansion and modernization of long term care facilities, society has seemed content to place the chronically ill and aged in these facilities even without much attention from health care professionals.

But the repository concept has not changed significantly. Health care professionals have made ineffective (weak) efforts to modernize care concepts in the new facilities. The medical profession has continued its previous emphasis on acute episodic illnesses which are treatable and curable. The highly trained scientific physicians of our time find incurable problems of the chronically ill and aged depressing and have abdicated responsibility for leading needed improvements in the care being provided. Physician placement of patients in Nursing and Boarding Care Homes has been haphazard—certifying admission to any nearby facility satisfactory to the family. State mental institutions virtually stopped admitting geriatric patients and discharged long term mental illness patients of all ages to community Nursing and Board Care Homes. Now 75% of the mentally ill are in these facilities and are almost totally neglected by the Mental Health Care Establishment.[9] Psychiatric hospitals, Psychiatrists and Community Mental Health Centers do very little for these patients. The average nursing home may contain a wide array of different kinds of patients, making optimum individualized care extremely difficult: e.g. there may be young and old psychotics, mentally retarded, neurological disease cripples, developmentally disabled, and recent discharges from acute hospitals needing active restorative care, all mixed with severely disabled and dying Old-Old patients. Here is advanced chronic disease of almost every conceivable type running its course toward inevitable death without serious concern by the physicians. It is no wonder mental deterioration is extremely prevalent and often developes rapidly.

Nationally about 5% of persons 65 or more years old are in Nursing or Boarding Care Homes. In Minnesota the percentage is about 6.5. As costs have risen and Medicare has reduced coverage, more and more of the patients have had to resort to the public poverty support system, Medicaid. Currently 62% of approximately 45,000 long term care patients in Minnesota are supported by Medicaid. Most are over age 65 but 22% are younger: the Mentally Retarded and Mentally Ill from State Mental Institutions.

Minnesota has no Chronic Disease Hospitals and all but a few of the 73 Convalescent and Nursing Care units of general hospitals function for custodial care rather than for restoration and rehabilitation. Return to independent living has not received sufficient attention!

External Peer Review of the 28,000 Medicaid patients in 575 Long Term Care Facilities by the Minnesota Department of Health has identified two principal problem areas:[10] (1) Comprehensive pre-placement examinations with medical plans for optimum care, and (2) Coordinated psychiatric or psychosocial evaluation and plans for care for the 63% of all Medicaid patients found to have mental illness or disability.

Why Is the Specialty of Gerontology and Geriatrics Needed?

A chronically ill and disabled person is a multiproblem patient and the traditional single system medical approach is not applicable.[11] Physical and psychological problems co-exist and the two frequently create a physiological feedback mechanism. The physician needs to make situational diagnoses with inclusion of social, economic, medical and psychological elements.[12] National studies have shown that residents of Nursing and Boarding Care Homes have an average of 2.5 chronic conditions and 25% of them have five or more.[13] In Minnesota, Skilled Nursing Facility Medicaid patients had an average of 3.4 diagnoses apiece and 25% had five or more. Circulatory system and neuropsychiatric disorders were present in over half of all long term Medicaid patients.[10]

In one study of the accuracy of medical diagnoses of 100 patients admitted by 50 different physicians, the primary diagnosis on admission to the Nursing Home was inaccurate in 64% of the patients and secondary diagnoses were either lacking or inaccurate in 84%.[3] There were no significant differences between patients admitted from acute hospital, psychiatric hospital, home or another long term care facility. The history and physical recorded in nursing home charts are frequently little more than the hospital discharge summary of the most recent acute episode. The labels Chronic Brain Syndrome, Senile Dementia and Cerebral Arteriosclerosis are applied all too frequently without diagnostic evaluation. Studies have shown that Chronic Brain Syndrome is often used erroneously in treatable depression and other functional psychiatric disorders.[14] Subclinical or mildly clinical Chronic Brain Syndrome is exacerbated frequently by aggressive use of sedatives, hypnotics, psychotropic drugs and inadequate treatment of chronic heart failure and infections. Older patients have reduced tolerance to many drugs. The tendency for them to be given four, five or more different drugs for multiple symptoms greatly increases the risk of potentiation or cross tolerance.

On the average, Medicaid patients in Skilled Nursing Facilities in Minnesota in 1974 had prescriptions for six oral medications and took seven doses per day.[15] However, 25% of the 9000 SNF patients were receiving 10 or more doses per day (1% received more than 20 doses per day.)

An "in depth review" of drug utilization patterns in five Skilled Nursing Facilities revealed four problem areas: (1) more prescription orders were received over the phone or by mail than in the nursing home; (2) many "p.r.n." drug orders were administered routinely with no recorded justification; (3) many patients on long term multiple drug therapy received no laboratory tests; and (4) many patients on toxic drugs were not being monitored for possible toxic effects.[16]

A similar review of psychological disturbances in another sample of SNF's showed: (1) an 85% incidence of psychiatric disorders; (2) a 67% incidence of missed or incorrect psychiatric diagnoses; (3) inadequate psychotropic medication regimens which were largely on a "p.r.n." basis;

and (4) a lack of understanding of psychopathology and treatment of psychologic disturbances by physicians, nurses, nursing assistants and relatives.[16]

One author has recently emphasized: few physicians are trained in long term management of chronic illness, home care and other facets of geriatric care. He concludes medical education must be redesigned to include these.[17]

In the Age of Darwin and Freud, where developed countries are moving toward zero-population growth and most persons will live beyond the Biblical "three score and ten," there must be re-definitions of health and the mission of health care professionals.[1] The still prevalent concept of health as the absence of disease and pathology is obsolete. Freymann defines health as the presence of social functioning; i.e. the ability to cope, and control one's environment to the maximum extent possible within the constraints of nature and circumstance. The mission of health care professionals should be defined as preservation for the maximum number of health-years within the constraints of available biologic and socio-economic resources.[1] These definitions, though seldom expressed, are the viewpoints of most of the middle aged and elderly in our population today. Society is asking for health care trustees who will assume the broadest responsibilities and demonstrate the broadest vision in management of health care services, to produce a maximum number of health-years and follow through with personal guidance and concern to the ultimate desire of death with dignity.[18] Physicians require special training in Gerontology and Geriatrics if they are to continue to be the health care trustees in the coming years. Social, moral and ethical issues and social expectations of the role of the patient's trustee or personal advocate must be emphasized.

Where Will Optimum Geriatric Care Be Provided and Taught?

Great Britain has a well developed system of Geriatric Care Centers as an integral part of the general hospital system. The Centers include in-hospital care, hospice sections for terminal illness, Geriatric Day Hospital Care, special units for complete assessment of chronic illnesses and arrangements for supportive services, direct relationships with long term care facilities and extensive outreach support services.[19] Geriatric specialists are in charge and every effort is made to keep the patients living as normally as possible in the community. Out-reach support services in Scotland are estimated to be eight times as great as they now exist in this country.[19] In contrast we still place primary emphasis on institutionalization of patients in hospitals or in long term care facilities.

However, America has begun to respond to the needs for more comprehensive services for the chronically ill and aged. A prime example is the progressive new programs for the Developmentally Retarded. Emphasis is placed on normalized living in residential facilities, evaluation of each resident by a multidisciplinary professional team, and goal oriented treatment and activity programs to promote maximum self-care and independence by each individual. The needs of the elderly are similar and the methods being employed could be readily adapted.

Teaching programs in Geriatrics are being developed in many areas of the country but they vary widely in type and degree of comprehensiveness. Some are in teaching hospitals[20,21] some in community hospitals, some in nursing homes and some in community geriatric centers. No uniformity exists as to the content of Geriatrics or how it should be taught.

Summary

The art and science of Geriatrics and Gerontology need to be developed, and indeed are being developed, as a distinct medical discipline —"this should involve accurate assessment of the diagnosis, the amount of disability, the potential for recovery of function, the relative balance of emotional versus physical disability and the application of such information toward the objective of returning the patient to his own community with sustained capacity to carry out the activities of daily living."[22]

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1. Freymann JG: The American health care system: its genesis and trajectory. Medcom Press, 2 Hammarskjold Plaza, NY, NY 10017, 1974.
2. James G: The general practitioner of the future, New Engl J Med 270:1286, 1964.

3-22. Will be found on page 686.

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(Coninued from page 722)

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MD AVAILABLE FOR LOCUM TENENS IM or ER, board eligible (Mayo), full time April, May and June 1977. Married. Minimum $1,000/wk, prefer near Rochester but anywhere. CV request, RRI Dodge Center 55927. (374-2453).

INTERNIST—Excellent opportunity for active practice of general internal medicine. Four-man group in North Iowa. Midway between Des Moines and Mpls. Close to Lake. Excellent art museum and school system. Starting salary $40,000, plus bonus. Modern hospital. 35,000 community with 100,000 drawing area. Phone collect at 515-423-0244.

FOR SALE or lease—Completely equipped Dr's office, south Mpls suburb. Available immediately. Established practice 20+ years. Contact: M. L. Lindblom, M.D., 101 So. University Dr., Apt. 102, Fargo, No. Dak. 58102. Phone: 701-235-5830.

ST. CROIX HEALTH CENTER—New Richmond, Wisconsin. *Psychiatrist-Clinical Director*—Full-time position in a comprehensive center operating in-patient and out-patient mental health programs, in-patient and out-patient alcoholism treatment programs, and programs for the developmentally disabled, including adult day care and sheltered work. Salary is negotiable depending upon background and experience. The facility is situated in a town of 4,000 population 35 miles from downtown St. Paul, Minnesota. Contact—Sumner Bright, Program Director, St. Croix Health Center, Box 99, New Richmond, Wisconsin 54017. Phone (715) 246-6186.

OB-GYN, ENT, PEDIATRICS SPECIALISTS needed by 16-man multi-specialty clinic in university community of 50,000 in western Wisconsin; excellent retirement and fringe benefits; fine recreational opportunities; salary negotiable. Send curriculum vitae and references to: John R. Ujda, M.D., La Crosse Clinic, 212 South 11th Street, La Crosse, Wisconsin 54601.

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INTERNIST WANTED with Cardiology training to join small group in Southern Idaho. For particulars call or write to: Dr. John H. Affleck, 231 4th Ave. No., Twin Falls, Idaho 83301. (Telephone: 208 733 9111 (or) 208 733 5762.

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Continuing Medical Education

Clinical Cardiology Conference

An innovative multimedia teaching program in clinical cardiology will be brought to Twin City Family Physicians, and Internists from October 11th through October 23rd by Roche Laboratories. Drs. W. Proctor Harvey and Antonio deLeon, Georgetown University Division of Cardiology, simulate actual patient work-ups and afford the participants with all the necessary parameters to make a diagnosis. These include Xrays, simultaneous heart sounds, actual electrocardiograms, phonocardiograms and catheterization data. These work-ups, through the use of coordinated audiovisual equipment, give the observer a unique educational presentation. The series includes:

- Art of Auscultation.
- Auscultatory Roulette.
- A Patient with Systolic Murmur.
- A Case of Unexplained Heart Failure.
- A Patient with a Systolic Murmur: Innocent vs. Significant.
- Restenosis of the Mitral Valve.
- Also featured is Dr. Alan Lyon, Director of Medicine-Brookdale Hospital Center-Brooklyn, N.Y., in *Interpreting Heart Sounds.*
- Abnormalities of the First and Second Heart Sounds.
- Extra Heart Sounds Other than Murmurs.

Conference institutions include:

October 11 (am)-St. Johns Hospital, Robert W. Reif, M.D.
October 11 (pm)-St. Paul Ramsey Hospital,-David Paulson, M.D.
October 12-Group Health
October 14-St. Joseph's Hospital, A. Richards, M.D.
October 15-Miller Hospital, Richard Guiton, M.D.
October 18, 19-Hennepin County Medical Center and Metropolitan Medical Center, Arthur Leonard, M.D.
October 22-Bethesda Lutheran Hospital, Don Asp, M.D.. Frank Indihar, M.D.

Program information will be posted in the doctor's lounges.

Contact your Director of Medical Education for additional data, concerning schedule content and attendance.

Ninth Annual North Memorial Medical Center
OG-GYN Symposium
December 3, 1976

Symposium will be held in the North Memorial Medical Center Auditorium, and the following is a tentative program:

Norman F. Gant, M.D.—University of Texas
Roy M. Pitkin, M.D.—University of Iowa
Jack R. Robertson, M.D.—Santa Maria, California
Douglas R. Shanklin, M.D.—University of Chicago
Barry S. Schifrin, M.D.—Los Angeles, California

Contact: Doctors Milton Baker and Harry F. Farb, North Memorial Medical Center, 3220 Lowry Avenue North, Minneapolis 55422.

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North Central Medical Conference 698
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Roche Laboratories .... Cover 2, 663. Covers 3-4
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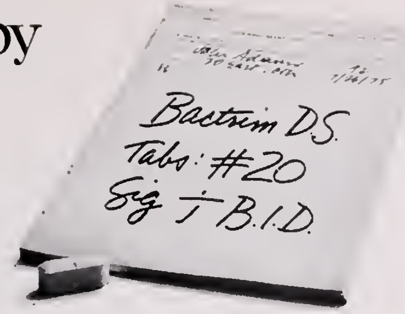
10-day Bactrim therapy outperforms 10-day ampicillin therapy.



Bactrim DS.
Tabs: #20
Sig ī B.I.D.

In a multicenter, double-blind study of patients with chronic or frequently recurrent urinary tract infection, Bactrim 10-day therapy outperformed ampicillin 10-day therapy by 27.2%, when comparing patients who maintained clear cultures for eight weeks. Criterion for "clear culture" was 1000 or fewer organisms/ml of urine.

While adverse reactions noted in this study were mild (*e.g.*, vomiting, nausea, rash), more serious reactions can occur with these drugs. See manufacturer's product information for complete listing. Maintain adequate fluid intake; perform frequent CBC's and urinalyses with microscopic examination.

Note: Bactrim tablets were used in these clinical trials. Bioequivalency studies show one Bactrim DS double strength tablet is equivalent to two Bactrim tablets.

Bactrim™ DS

(160 mg trimethoprim and 800 mg sulfamethoxazole)

Double Strength tablets
Just 1 tablet B.I.D.

Bactrim™

(80 mg trimethoprim and 400 mg sulfamethoxazole)

2 tablets B.I.D.

For chronic or frequently recurrent cystitis and pyelonephritis due to susceptible organisms.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris* and *Proteus morganii.*

NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections. The recommended quantitative disc susceptibility method (*Federal Register, 37*:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **Data are insufficient to recommend use in infants and children under 12.**

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) every 24 hours
Below 15	Use not recommended

Supplied: Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole — bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10.

Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole; fruit-licorice flavored — bottles of 16 oz (1 pint).

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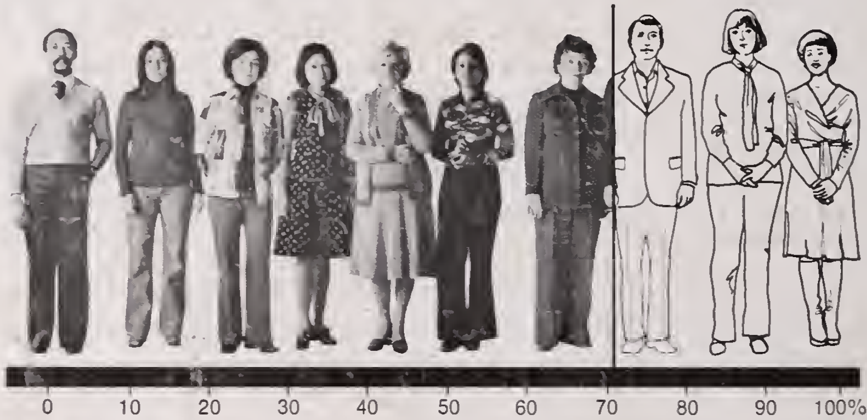
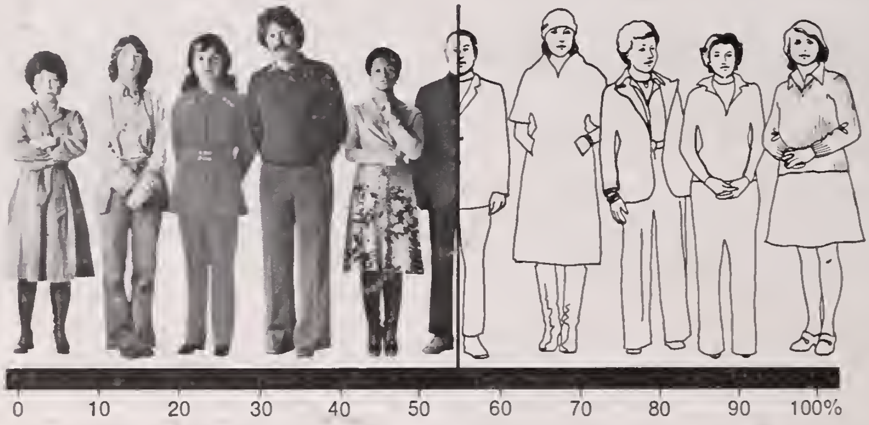
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

In a multicenter study of patients with chronic or frequently recurrent urinary tract infections

Bactrim was 27.2%* more effective than ampicillin in keeping patients infection-free for 8 weeks.†



Bactrim–70.5% of 78 patients infection-free at 8 weeks.



ampicillin–55.4% of 74 patients infection-free at 8 weeks.

*This percentage is arrived at by the statistical method of dividing the difference between Bactrim and ampicillin results (15.1%) by the percent of ampicillin results (55.4%).

†Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

Bactrim™ DS

(160 mg trimethoprim and 800 mg sulfamethoxazole)

Double Strength tablets
Just 1 tablet B.I.D.

Note: Bactrim tablets were used in these clinical trials. Bioequivalency studies show one Bactrim DS double strength tablet is equivalent to two Bactrim tablets.

Please see summary of product information on preceding page.

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Gerald E. Cotton, M.D.

NOVEMBER 1976

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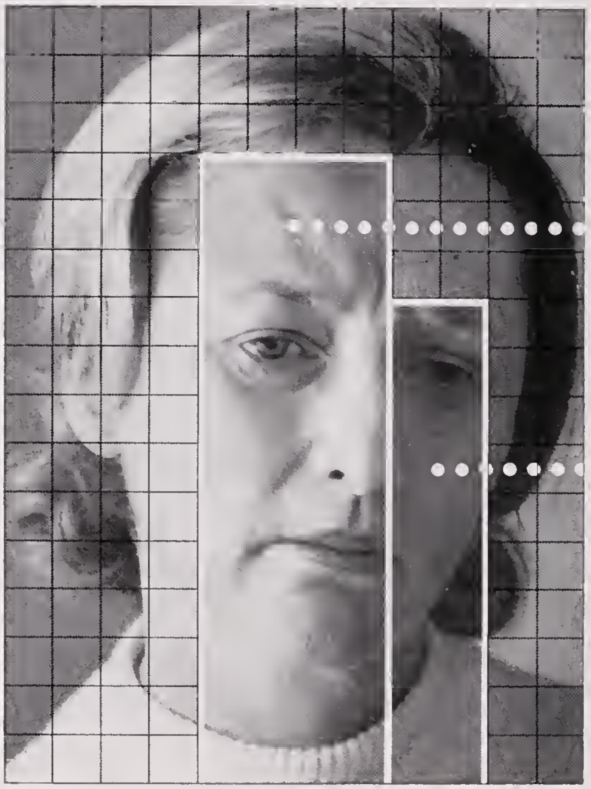
Predominant psychoneurotic anxiety
Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in freque
and/ or severity of grand mal seizures r
require increased dosage of standard a
convulsant medication; abrupt withdra
may be associated with temporary in-
crease in frequency and/ or severity of
seizures. Advise against simultaneous i
gestion of alcohol and other CNS depres
sants. Withdrawal symptoms (similar to
those with barbiturates and alcohol) ha
occurred following abrupt discontinuan
(convulsions, tremor, abdominal and m
cle cramps, vomiting and sweating). Ke
addiction-prone individuals under caref

respond to one

According to her major
iptoms, she is a psychoneu-
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iety. But according to the
cription she gives of her
ings, part of the problem
y sound like depression.
s is because her problem,
hough primarily one of ex-
ive anxiety, is often accom-
ied by depressive symptom-
logy. Valium (diazepam)
provide relief for both—as
excessive anxiety is re-
ed, the depressive symp-
is associated with it are also
n relieved.

There are other advan-
es in using Valium for the
nagement of psychoneu-
c anxiety with secondary
ressive symptoms: the
chotherapeutic effect of
ium is pronounced and
id. This means that im-
vement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

Valium® (diazepam) Ⓘⓥ

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

'eillance because of their predisposi-
to habituation and dependence. In
gnancy, lactation or women of child-
ring age, weigh potential benefit
nst possible hazard.

:autions: If combined with other psy-
tropics or anticonvulsants, consider
fully pharmacology of agents em-
ed; drugs such as phenothiazines,
otics, barbiturates, MAO inhibitors
other antidepressants may potentiate
ction. Usual precautions indicated in
ents severely depressed, or with latent
ression, or with suicidal tendencies.
Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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President's Letter

Violence on TV

There may not yet be a scientifically valid link between what children see on television and real life crime, but there is cause for deep concern on the part of physicians and parents alike.

When we look at recent published statistics referring to violence on TV such as: the average child witnessing 18,000 murders and many more detailed crimes before graduation; that they spend more time watching television, 15,000 hours as compared to 11,000 hours in the classroom; that cartoons show one incident per minute of robbery, arson, bombing, forgery, smuggling, beating, and torture, and that there is six times more violence during one hour of children's television than adult television, we should be pleased at the definitive action taken by the AMA House of Delegates at their recent annual meeting in Dallas, Texas. The House of Delegates recommended that the AMA publish a booklet which will be available soon for physicians to distribute to their patients suggesting what parents should look for in television programming. A committee to evaluate research on TV violence was set up. They have urged the National Institute of Mental Health to provide monies for research and have requested the Federal Communications Commission to use violence indices in program listing for parents. Finally the AMA has suggested periodic meetings with the National Association of Broadcasters to discuss the impact of television on children. The NAB code directs itself to responsibilities in all these areas, but it only resulted in a public relations document which never was intended to guide actual practices.

The Surgeon General's Report of 1972 on Violence on TV came to similar conclusions. However, seven individuals with outstanding reputations in research in this field were replaced on the Fact Finding Committee by five television network executives, and the resultant summary became misleading with words such as: preliminary, tentative, howsoever, and casual relationships, thus watering down the conclusions.

One hundred forty-six articles in Behavioral Science Journals representing fifty studies involving 10,000 children and adolescents from every conceivable background showed that violence viewing produces increased aggressive behavior in the young and immediate remedial action in terms of TV programming is warranted. Studies have suggested that novel aggressive behavior sequences are learned by children through exposure to television if practiced once, if found in a familiar life setting, or not punished, and when it was a favorite method to obtain goals. Decreased emotional sensitivity to media violence from repetition has also been demonstrated. There has been no evidence that the continued observation of pain, horror, and suffering results in catharsis, but aggression can be inhibited by reminders that the aggression was morally wrong and an awareness of the bloodly painful aftermath was clearly depicted.

While we are waiting for the pamphlets to be printed and distributed and for the Federal Communications Commission to force compliance on the National Association of Broadcasters of its new guidelines of January 1, 1976, there is much that we as individual physicians can recommend to parents to guide them to selective TV programming.

Parents should ask themselves: Does the program appeal to the audience for whom intended; does it present racial groups positively; does it present social issues that are appropriate for a child; and does the program encourage worthwhile beliefs, ideals, and values. Parents should ask themselves if the program stimulates constructive activities, separates fact from fantasy. and does it contain artistic qualities. In other words. parents should keep control of the television set, monitor the programs, discuss its contents with their youngsters, and finally set a good example and find other experiences for themselves and their children. Maybe with pressure from parents, teachers, and physicians the television industry will get off its current violence kick and get on with the job of creative programming.

Children have neither money nor vote and no political constituents. To be silent is to acquiesce, and it is clear that if we truly care about our children we cannot be silent.

Richard E. Anonsen, M.D.
President
Minnesota State Medical Association

WE NEED YOU

Every once in a while a cause of unusual merit comes along. Such a one is the drive to increase the resources of the Minnesota State Medical Association Foundation Student Loan Fund.

For more than 15 years this Foundation's activity has given witness to the interest of practicing physicians in those who will one day stand in their shoes. We can all take pride in the record.

Two hundred twelve interest-free loans have been provided to needy students. We can all be proud of the default-free record of repayment by the young people who have been aided by the M.S.M.A.

Bad times have come upon the fund, for while these loans do draw interest after graduation and the fund assets do grow slowly, the need for student assistance grows more rapidly. Everything is up: tuition, books, fees, living costs . . . everything but student financial support. As many of the traditional sources of aid have eroded, more students are turning to their seniors in the profession to help them through their training period. As a result your fund assets are completely disbursed in student loans.

Currently, thirty medical students have applied for assistance and more, we are certain, will be along later. Many will not be accommodated unless the resources of this fund are augmented.

If every Minnesota physician made a tax deductible contribution of $100 to the M.S.M.A. Foundation Student Loan Fund, the problem would be solved. The worthy young men and women who so badly need our help would find a ready and understanding ally.

An organized drive is underway. YOUR HELP IS NEEDED. Contribute today and contribute generously.

John Regan, M.D.
Chariman

Minnesota Urological Society Pyelogram Conference

Friday, November 19, 6:30 p.m. L'Hotel Sofitel. Contact: S. J. Antolak, Jr., M.D., Secretary-Treasurer, 228 Lowry Medical Arts Building, St. Paul 55102.

Editor's Notebook

A Collection of Syndromes

Spasmodically the urge may seize you to start a new project, conquer a new sport, or remodel your body. Suppose this urge does not pass. Suppose it persists, and you feel compelled to do something. Well, for you I have collected a series of articles on syndromes of new activities. These articles may discourage you from embarking on any foolhardy new venture.

Frisbee Finger

The frisbee, as you know, is the common man's discus. You may want to have a fling at it because it is practical, inexpensive, and good exercise. Besides, you can do it anywhere. Well, almost anywhere.

But beware of the "frisbee finger."[1-3] Throw a frisbee too often, and you abrade the middle finger of your throwing hand, with or without associated clear vesicles distal to the abrasion and vesicles on the thumb of the same hand. You can bandage or tape the finger and thumb, but accuracy suffers. If you're seeking temporary relief, you can soak the affected digits in cold beer. The frisbee, my sources make clear, is not something to be tossed around lightly.

Yoga Foot Drop

Rather than be frivolous with a frisbee, you might want to turn to something more profound: yoga. Yoga is a means of mind control. Yoga teaches that a dormant divine potency at the base of the spine is linked to psychic centers. To activate this potency and to control yourself you assume a well-known Yoga pose—the Vajrasan or kneeling pose, in which you sit on your heels with your spine erect. Which sounds good, particularly the sitting on the heels part.

Unfortunately, you may suffer an embarrassing indignity. A New York physician reports if you sit on your heels for too long, you may injure both common peroneal nerves.[4] Bilateral foot drop follows, and you may not be able to rise, to or for any occasion.

Conganuria[4]

Yoga may be too meditative anyway. Maybe you want to try something more vigorous, like pounding on a Conga drum.

According to the literature, drums can be bad, too. Three articles say overzealous congo drumming causes hemoglobinuria and myoglobinuria.[5-7] Perhaps you should drum up other things to do.

Karate Chops

What about karate? You might have bricks and boards lying around the backyard, and with karate, you could break sticks and stones with your bare hands.

But you can also break your own muscles, with associated myoglobinuria.[8] And your opponent, if he hits you right, can lacerate your liver.[9] You are interested in self-defense, not self-destruction.

Other Activities

As you consult the literature, you will realize nothing is safe (or sacred):

Other Activities	Syndrome or Injury
Reading[10]	Toilet seat neuropathy (sciatic nerve)
Helping with household duties[10]	Grocery bag neuropathy (radial nerve) Housemaid's knee (prepatellar bursitis)
Practicing guitar[10]	Guitarist's palsy (common peroneal nerve)
Wearing ski boots[10]	Ski-boot neuropathy (S_1 sensory nerves)
Toting a six-shooter[10]	Gun-belt neuropathy (lateral femoral cutaneous nerve)
Sleeping at the bar	Saturday Night palsy (ulnar nerve)
Walking or hiking[11]	March or stress fracture
Jogging[11,13]	Tenosynovitis, tendonitis, shin splints anterior tibial syndrome, hamstring pull, foot strain, sudden death
Tennis[11,18,19]	Tennis elbow, tennis leg, detached retina
Golf[11]	Golfer's elbow, golfer's ear, acute and chronic frustration and depression, and liver disease
Surfing[12]	Surfer's nodules (knee ulcers)
Barbecuing in the backyard[16]	Backyard barbecue syndrome
Hang gliding[17]	Multiple fractures
Skateboarding	Broken tibia

Chinese Food Ingestion

Clearly, then, popular sports and household tasks have their hazards. What is left? Eating, of course, particularly eating foods of other countries. After all, learning about other foods expands your mind, teaches you other customs, and educates the palate, and may even slim your body.

But eating too can be hazardous.

Consider the Chinese Restaurant syndrome.[14,15] If 15 to 25 minutes after eating a Chinese meal, you have a burning sensation in the back of your neck, followed by burning over your face, arms, and chest you are experiencing the Chinese Restaurant syndrome. The cause is monosodium glutamate, a condiment and preservative often used in Chinese cooking.

Conclusion

If this rambling essay has any conclusion, and I don't see why it deserves any, I suppose it is this: new projects can be hazardous to your health, and usually are. Practically nothing new you can do these days is worth the risk.

Richard L Reece MD

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Minnesota State Board of Medical Examiners

1976 Minnesota Session Laws Chapter No. 222 provides as follows:

Section 40. Minnesota Statutes 1974, Chapter 147, is amended by adding a section to read:

(147.074) (Filing of hospitals served) *Each physician shall file with the board a list of the in-patient and out-patient medical care facilities at which they have medical privileges. This list shall be updated when the physician applies for license renewal.*

This list must be submitted to the Board with your 1977 annual registration payment. Forms will be mailed to you with the annual registration renewal form.

Loren E. Nelson, M.D.
Secretary-Treasurer

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Contents—November, 1976

Volume 59:11
Pages 735-822

COVER PHOTO—"The Christian Radich"
Gerald E. Cotton, M.D. ... 752

PRESIDENT'S LETTER—Violence on TV
Richard E. Anonsen, M.D.
President, Minnesota State Medical Association ... 739

EDITOR'S NOTEBOOK—A Collection of Syndromes
Richard L. Reece, M.D., Editor-in-Chief ... 741

ORIGINAL CONTRIBUTIONS

Diagnosis of Mild Diabetes
Frank Q. Nuttall, M.D., Ph.D. ... 747

Management of Unstable Diabetes
Edward G. Lufkin, M.D. ... 753

Acute Diabetic Complications
Bruce R. Zimmerman, M.D. ... 757

Renal Transplantation in the Diabetic
David E. R. Sutherland, M.D., et al. ... 766

Management of the Pregnant Diabetic
Robert F. Coniff, M.D. and Edward C. Maeder, Jr., M.D. ... 772

Research in Human Diabetes—1976
Frederick C. Goetz, M.D. ... 779

Diabetes Mellitus—A Plan for the Physician and His Patient
G. E. Cotton, M.D. ... 784

Education of the Diabetic Patient
Carelyn P. Fylling, R.N., M.S. et al. ... 789

EDITORIALS

Arnold Lazarow, M.D., Ph.D. (1916-1975)
Rachmiel Levine, M.D. ... 797

Diabetes Mellitus—1976
G. E. Cotton, M.D., Guest Editor ... 799

Help Your Diabetic Patients—Make Them Aware of ADAM
Donald R. Moberg, President
American Diabetes Association of Minnesota ... 800

Management of the Pregnant Diabetic
Peter E. Fehr, M.D. ... 801

Blood Glucose Control in Diabetes
George F. Cahill, Jr., M.D., President
Donnell D. Etzwiler, M.D., President-Elect
Norbert Freinkel, M.D., Vice President
American Diabetes Association ... 803

MSMA HIGHLIGHTS—1976 MSMA Socio-Economic Conference ... 808

CONTINUING EDUCATION ... 740, 743, 756, 793, 805, 822

CLASSIFIED ADVERTISING ... 817

INDEX TO ADVERTISERS ... 822

MINNESOTA MEDICINE REPRESENTS

Association of Neurologists of Minnesota
Duluth Surgical Society
Hennepin County Psychiatric Society
Minneapolis Academy of Medicine
Minneapolis Surgical Society
Minnesota Academy of Family Physicians
Minnesota Academy of Medicine
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Diagnosis of Mild Diabetes

FRANK Q. NUTTALL, M.D., Ph.D.

Overt diabetes mellitus is easily recognized and does not offer a problem in diagnosis. However, mild diabetes is difficult to diagnose with certainty. Many factors may influence glucose tolerance. Because of this we urge caution in diagnosing diabetes when minor abnormalities are noted. Only if the results are abnormal on repeated occasions and in the absence of recognized causes of abnormal tolerance should the diagnosis be made. In patients at bed rest and in the elderly, particular caution should be used.

DIABETES MELLITUS has been known since antiquity. However, in spite of intensive investigation the disease is poorly understood and cannot as yet be readily defined. The most general and probably most satisfactory definition is that it is a chronic condition in which there is an abnormally high circulating glucose concentration in the fasting state and/or following the ingestion of a standard amount of glucose. The pathogenesis of the abnormal glucose concentrations is a reduced or absent physiological effect of insulin. As pointed out by Dr. Cotton elsewhere in this issue,[†] not all diabetics have a reduced ability to secrete insulin. In fact, circulating insulin concentrations actually may be increased in many obese diabetic patients[1] and in other so-called insulin resistant diabetics (lipoatrophic diabetes),[2] myotonia dystrophica.[3] Diabetes, then, is not a single entity but rather represents a number of disease states having in common an abnormality in glucose and insulin metabolism.

Diabetes can be classified into two large groups. So-called primary, "true" or idiopathic diabetes in which the etiologies are uncertain but in which heredity appears to play an important role and the secondary diabetes in which the cause of the elevated circulating glucose concentration is apparent. In this latter group is included destruction of islet tissue (surgical removal or tumor infiltration of the pancreas, chronic pancreatitis and hemochromatosis) hepatic insufficiency, uremia and glucose intolerance induced by over production of hormones whose effects are physiologically antagonistic to the effects of insulin (growth hormone, cortisol, glucagon, catecholamines) or which inhibit secretion (epinephrine).

When the term "diabetes" is used without qualification, primary or idiopathic diabetes is implied. This is how the term will be used in the discussion to follow. Thus, diabetes (idiopathic) can be considered to be a diagnosis of exclusion.

There is no problem in diagnosing severe insulin-dependent type diabetes. Generally the patients present with grossly elevated plasma glucoses, are very ill, dehydrated and usually in ketoacidosis. However, the diagnosis of mild insulin-independent type diabetes often is very difficult. Generally they are asymptomatic or only minimally symptomatic. In these patients the criteria to be used for diagnosis are controversial and of necessity somewhat arbitrary. This is because it is impossible by any criteria to clearly separate a diabetic population from the population at large unless the diabetes is overt.

In Table 1 are listed tests that have been used to diagnose diabetes. The last five of these are rarely used at the present time. The cortisone-glucose tolerance test was developed as a research procedure to increase the sensitivity of the standardized glucose tolerance test. It rarely has been used clinically. The intravenous glucose tolerance test is less sensitive than the oral glucose tolerance test and is used only when a patient cannot take glucose orally. Several different techniques for doing the test have been described but the one reported by Dyck and Moorhouse[4] appears to

---

[*] Chief, Metabolic-Endocrine Section, Veteran's Hospital, Minneapolis and Professor of Medicine, University of Minnesota, Minneapolis.

[†] See page 784.

be the most discriminatory. The tolbutamide test no longer is used to diagnose diabetes because it also lacked sensitivity.

TABLE 1

Tests Used to Diagnose Diabetes Mellitus

1. Fasting plasma (serum) glucose
2. Two hour postprandial plasma glucose
3. Standardized glucose tolerance test
4. Cortisone-glucose tolerance test
5. Intravenous glucose tolerance test
6. Tolbutamide test
7. Serum insulin determination
8. Urine glucose

When serum insulin determinations became available it was hoped that they would be of great value in diagnosing diabetes, but the results have been disappointing. There is a great deal of overlap between patients with diabetes and normal individuals. As mentioned previously, many diabetics, particularly obese diabetics, have a normal or even high serum insulin concentration both fasting and after glucose administration. There is considerable evidence that the early phase of glucose induced insulin release is reduced in even mild non-insulin dependent diabetics[5] but so far this observation has not been diagnostically useful.

Urine glucose testing is still a common way of screening for diabetes, but it should never be used as the only means of diagnosis. This is because the presence of significant glucosuria depends on the renal threshold. If the renal threshold is low, glucose will appear in the urine when the circulating glucose concentration is normal and the individual will be misdiagnosed as having diabetes. If the renal threshold is high, as occurs in patients with renal disease or in elderly persons, the diagnosis may be missed since the blood glucose may be elevated in the absence of significant glucosuria. A specific test for urine glucose should always be used, such as glucose oxidase impregnated paper strips.

The diagnosis of mild diabetes in the majority of cases depends on the demonstration of an abnormal fasting plasma glucose or two hour postprandial glucose concentration or an abnormal glucose tolerance test result.

Blood (Plasma) Glucose Determination

In order to properly interpret glucose results it is important to know how the glucose determination was done; the factors that may influence the results; and whether whole blood, plasma, or serum was used. Serum and plasma glucose concentrations are similar but higher than in whole blood. Red cells are freely permeable to glucose, thus the intracellular concentration of glucose will be the same as plasma. However, only approximately 72% of the red cell is water into which glucose can diffuse. The remainder is protein, stroma, and other particulate matter. This can be compared to plasma which is 94% water. A plasma or serum glucose concentration then should be about 10% higher than in whole blood. The difference, however, will vary with the hematocrit. This is one reason why plasma or serum glucose determinations are more reliable than those done in whole blood. Since the difference is a percent, it also is apparent that the difference will be greatest at high glucose concentrations. At 100 mg/dl the difference is 10 mg/dl, but at 300 mg/dl the difference is 30 mg/dl, etc. Ingram et al.[6] however, have found that the difference between plasma and whole blood values depended on the glucose method used. Using an Autoanalyzer-ferricyanide method the difference was 14% plus a constant of 6 mg/dl at all glucose concentrations, but with a Somogyi-Nelson or glucose oxidase method the difference was only 4%. The reason for this discrepancy was not explained.

Glucose Methods

Several methods for measuring glucose in body fluids, the chemical basis for the tests and the approximate normal fasting range for each are given in Table 2. Methods which are based on the reduction of copper from a cupric to a cuprous form may measure all reducing substances in blood and are not specific for glucose. However, by use of the proper conditions, glucose may be measured almost exclusively. An example of this is the Somogyi-Nelson procedure, a standard glucose procedure in use for the last 35 years. More recently, methods based on the oxidation of glucose to gluconic acid by the enzyme, glucose oxidase, have become popular. This enzyme for all practical purposes only uses β-D-glucose as a substrate, so methods based on this reaction have great specificity and also are very sensitive. However, high concentrations of ascorbic acid and bilirubin, hemolysis and uric acid inhibit the overall reaction.[7]

Probably the most widely used at the present time are the ferricyanide reduction and copper-neocuproine methods. This is because they have

TABLE 2
Methods for Measuring Whole Blood, Plasma or Serum Glucose

Method	Chemical Basis	Specimen	Approx. nl. range mg/dl
Somogyi-Nelson	$Cu^{++} + e \longrightarrow Cu^{+}$	whole blood plasma	60-100 65-105
Glucose oxidase	glucose + $O_2 \longrightarrow$ gluconic acid + H_2O_2 H_2O_2 + dye $\longrightarrow H_2O$ + color	whole blood plasma	60-100 65-105
Autoanalyzer	Ferricyanide + e $\longrightarrow$ Ferrocyanide (yellow) (colorless)	whole blood plasma	60-100 80-120
	$Cu^{++} + e \longrightarrow Cu^{+}$ Cu^{+} + neocuproine $\longrightarrow$ color	whole blood plasma	60-100 70-110
Ortho-toluidine	glucose + o-toluidine $\longrightarrow$ color	whole blood plasma	60-100 70-110

been adapted for use in the Autoanalyzer. These Autoanalyzer methods measure all reducing substances present in a dialysate of serum or plasma, and as a result would give higher values than with a so-called "true glucose method" such as the Somogyi-Nelson or glucose oxidase techniques. However, the dialysis system is arranged so that only a certain proportion of the total glucose actually gets measured. This plus the other reducing substances present gives a total value which is close to that obtained with the "true glucose methods" in normal individuals. In patients with uremia, however, spuriously high results may be obtained.[8,10] In 33 uremic patients Powell and Djuh[8] found a mean serum glucose concentration of 91 mg/dl when determined by a glucose oxidase method but a mean of 127 mg/dl when a ferricyanide or neocuproine method (SMA 6/60 or SMA 12/60) was used. This is a difference of 36 mg/dl. The mean BUN was 65 and the creatinine 12 mg/dl. It is obvious that considerable error is present with the latter methods when uremia is present. Under these circumstances mild diabetes may be misdiagnosed. On the other hand hypoglycemia would be difficult to detect. Presumably without any glucose present at all, the value obtained would be about 36 mg/dl. Recently methods based on the reaction of ortho-toluidine with glucose (aldohexoses) have been used with increasing frequency and also have been automated. The reaction is essentially specific for sugars and for all practical purposes measures only glucose. In uremic patients a spurious elevation may be seen but it is much more modest than with the above methods.[8] The ferricyanide method also gives higher values than the ortho-toluidine following glucose administration.[9]

Fasting Plasma (Serum) Glucose

If the plasma glucose is grossly elevated after a 12-14 hour fast on several occasions, the diagnosis of diabetes mellitus may be made without further diagnostic work-up. This is particularly true if the patient also has intermittent glucosuria. Whether the diabetes is primary or secondary to another disease state however, must be determined. A fasting glucose level above which the diagnosis of diabetes is highly likely cannot be given with certainty but values over 140 mg/dl on repeated occasions strongly suggest the diagnosis.

Two Hour Postprandial Glucose Determination

A two-hour postprandial glucose determination often has been used as a screening test for diabetes. It is done two different ways. Frequently the patient is merely told to eat his usual breakfast or a breakfast consisting of cereal and toast. A blood sample is obtained two hours later. The preferred method, however, is to have the patient fast overnight, then rapidly drink 100g of glucose solution. A blood specimen is obtained before and two hours after the glucose ingestion is begun. In general a normal plasma value is less than 140 mg/dl for individuals under the age of 50, but will depend on the method used. If the patient is known to have been eating a normal diet, has no other significant diseases and the glucose value is grossly elevated, 200 mg/dl or greater, diabetes is highly likely. If the result is not grossly abnormal, then a standardized glucose tolerance test should be done. If breakfast foods are used for the test the circulating glucose value is lower and a normal range has not been well standardized.[11]

Standardized Glucose Tolerance Test

The oral glucose tolerance test was first used in a standardized fashion by Hamman and Hirshman[12] in 1917 and since then it has been modified only slightly. In spite of all the advances in clinical medicine in the last fifty years, this test is still considered to be the best way of diagnosing mild diabetes mellitus.

Several methods for doing a glucose tolerance test and several ways of interpreting the results have been advocated. These are reviewed in reference 13. Probably the most widely used and best standardized is that developed by Fajans and Conn[14] (Table 3). The test was standardized using 111 subjects aged 20-39 without a family history of diabetes or large babies. An abnormal glucose tolerance was defined as a curve in which the whole blood glucose was 160 mg/dl (~185 mg/dl plasma) or greater at 60 minutes, 140 mg/dl (~160 mg/dl plasma) or greater at 90 minutes and 120 mg/dl (~140 mg/dl plasma) or greater at 120 minutes. These values all exceeded the mean by 2 standard deviations; that is, fewer than 2.5% of a normal population would be expected to have values above this level. However, several factors may influence the results.

TABLE 3
Oral Glucose Tolerance Test
(Method of Fajans & Conn)[14]

1. 300g CHO diet containing maintenance calories for 3 days
2. In a.m. of 4th day after a 12-14 hour overnight fast 1.75g glucose/kilo ideal body weight given orally (often just 100g given to all patients regardless of size)
3. Glucose is given as a lemon-flavored 25% solution
4. Blood and urine specimens obtained before and 30-60-90-120-180 minutes after glucose administered (often the 30 and 90 minute specimens are not obtained)
5. During the test the patient should remain in bed
6. Smoking is not allowed in the morning before or during the test

Factors that Influence Glucose Tolerance

Reproducibility

The reproducibility of the standardized glucose tolerance test has been studied by McDonald[15] in 334 normal prison inmates. A glucose tolerance test was done every two months for a year. An abnormal result was obtained in 10% of these men on at least one occasion but in none were the results consistently abnormal. Others also have noted considerable variability in normal individuals.[11] Because of biological variation the diagnosis of diabetes should only be made if the results are grossly abnormal. If modest abnormalities are present the test should be repeated at a later date. Only if the results are consistently abnormal should the individual be considered to be diabetic.

Glucose Load

Several investigators[11,16,17] have shown the importance of glucose load on the plasma glucose and insulin responses. It appears that 100 g gives a near maximal response in all individuals and is not different from the response to 1.75 g/kg. Amounts less than this however, result in lower plasma glucose and insulin concentrations. Thus, if a patient vomits up part of the glucose given, the test is invalidated.

Physical Activity

Prolonged bed rest diminishes glucose tolerance. The minimal duration of absolute bed rest before this is manifest is not known but it can be demonstrated after three days.[18] Approximately seven to 14 days are required for the effect of bed rest to disappear.[19] The mechanism of this is not known but it appears to be due to a decreased sensitivity to insulin.

Diet

It has been known since the mid-1930's that glucose tolerance is directly related to the quantity of carbohydrate in the diet.[20] The more carbohydrate the better the glucose tolerance in spite of variations in total caloric content. If dietary carbohydrate is less than 150g daily even normal persons may develop a diabetic-type glucose tolerance curve. These are the reasons for standardizing the carbohydrate intake at 300g daily for three days before the test. The variation in glucose tolerance with carbohydrate intake appears to be due primarily to a variation in sensitivity to insulin.[20] Prolonged fasting also causes deterioration in glucose tolerance.

Age

Glucose tolerance progressively diminishes with advancing age[11,21] and the criteria for normality in the standardized glucose tolerance test do not apply to subjects over the age of 50. Indeed, if the same normal range were used in subjects in this age group an abnormal result would be found in 30 to 100% of the individuals. Unfortunately, good data are not available on which to base normal diagnostic criteria for individuals over the age of 50. However, as a rule of thumb one should add 10 mg/dl to the upper limit of one hour and two hour post-glucose values per decade and use this as the upper limit of a normal range. As an example, if the two hour post-glucose upper limit is 140 mg/dl in persons up to the age 50 then the upper limit for a 50-59 year old would be 150 mg/dl and for a 60-69 year old it would be 160 mg/dl, etc. The reason for deterioration of glucose tolerance with age is not well understood. Fasting glucose concentrations also rise with advancing age, but the increase is relatively small (approximately 2 mg/dl/decade).

Potassium Deficiency

In 1961 Sagild et al.[22] induced 200-500 mEq K^+ deficits in normal men using a cation exchange resin and showed a definite impairment in glucose tolerance. This was true even when the serum K^+ concentration had not changed. This subsequently was confirmed by other investigators[23] and the mechanism was demonstrated to be an impairment in insulin secretion by the β cells. Since thiazide diuretics and furosamide lead to hypokalemia, these agents should be discontinued for at least a week before doing a glucose tolerance test.

Drugs

Thiazides, in addition to their hypokalemic effects, probably directly impair glucose tolerance. This has been noted in mild diabetics treated with triamterene, a thiazide which results in potassium retention.[24] Diazoxide, a non-diuretic thiazide, also is a potent inhibitor of insulin release and has induced hyperosmolar, hyperglycemic coma in non-diabetic individuals.[25] Dilantin also inhibits insulin release and with conventional doses may result in abnormal glucose tolerance.[26,27] In general it is best to discontinue all drugs which are not absolutely necessary for the patient's well being before doing a glucose tolerance test.

Non-endocrine Diseases

A number of clinical abnormalities are associated with abnormal glucose tolerance. These include trauma, burns, surgery, infections and other inflammatory diseases, acute myocardial infarction, cerebrovascular accidents, liver disease and uremia. In general, the mechanism appears to be insulin resistance as a result of an increased secretion of insulin antagonistic hormones but also may result from some impairment in insulin release.

Antifertility Agents and Pregnancy

Administration of estrogenic hormones is known to result in abnormal glucose tolerance in some women.[28] Pregnancy also may cause deterioration in glucose tolerance.[29] Insulin resistance and high circulating insulin levels have been noted in both groups.[30,31,2] Progestins also may reduce glucose tolerance but the mechanism is unknown.[28] If mild diabetes is suspected during pregnancy, it is best to repeat a glucose tolerance test sometime postpartum. In women on birth-control pills the drug should be discontinued for at least 4 to 6 weeks before repeat testing.

It can be seen that many factors influence glucose tolerance. Unless these are understood an erroneous diagnosis of diabetes may be made. The term "diabetes" carries with it the implications of a life-long disease and has many social, psychological, economic, and medical ramifications. Thus, the diagnosis cannot be taken lightly. Only when glucose tolerance is clearly abnormal on several occasions under standardized conditions should the diagnosis be considered firm. It also should be made with caution in patients at bed rest, in the elderly and in the presence of other significant diseases.

Some question the need for doing glucose tolerance tests at all and will only diagnose diabetes when the fasting plasma glucose value is consistently elevated.[32] They point out that mild glucose intolerance has not been demonstrated to be a coronary risk factor and in general is not associated with clinically significant microangiopathy such as diabetic retinopathy.[32] There also is little evidence that early diagnosis and treatment of mild diabetes improves mortality.[33]

This philosophy, I believe, is excessively nihilistic. In part it is based on our lack of good information regarding the long term course and complications of patients with mild diabetes and the lack of a treatment regimen which restores glucose and insulin metabolism completely to normal. Asymptomatic, non-insulin dependent diabetes, which includes some individuals with greater glucose intolerance, is associated with accelerated arteriosclerosis and a greater frequency of peripheral vascular and coronary artery disease.[34] Until the diseases manifesting themselves as idiopathic glucose intolerance are better understood, I believe the procedure should continue to be done. The glucose tolerance test at least will detect individuals at increased risk for hyperosmolar, hyperglycemic non-ketotic coma and for overt diabetes. Also whether a physician chooses to diagnose these patients as having abnormal glucose tolerance or diabetes is really a matter of personal preference.

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Cover Photograph

"The Christian Radich"

Dr. Gerald Cotton took the picture of the Norwegian Tall Ship "Christian Radich" as it left the Harbor of the Port of Duluth, August 12th. He used a Pentax Camera with Ektachrome 160 ASA film.

Dr. Cotton is an Assistant Professor of the Clinical Sciences, University of Minnesota Medical School, Duluth. His hobbies are: photography, metal working, welding, woodworking, hunting and fishing.

Management of Unstable Diabetes

EDWARD G. LUFKIN, M.D.*

Unstable diabetes is almost always caused by errors in treatment either on the part of the patient or professional personnel. Meticulous attention to details of diet, testing of urine sugar, and administration of insulin in proper form and dose usually results in improved control. A small group of patients continue to have unstable diabetes despite the most meticulous attention to treatment. The term "brittle diabetes" should be restricted to these patients.

UNSTABLE OR LABILE diabetes is an uncommon form of insulin-dependent diabetes mellitus characterized by excessive swings in blood sugar levels, frequent hypoglycemic reactions, and a tendency to severe hyperglycemia and ketoacidosis.[1] This variety is usually seen in slender patients, more commonly in children. In most instances of unstable diabetes, satisfactory control can be achieved by careful attention to routine diabetic techniques. However, there are a few patients whose diabetes is highly unstable despite meticulous attention to diabetes care. These are termed brittle diabetics.

Causes of Instability

The hormonal abnormality usually is deficiency of immunoreactive insulin, basally or after stimulation with various secretagogues.[2] Constant infusion of small amounts of insulin, with transient increases at mealtime, has been shown experimentally to stabilize patients with brittle diabetes.[3] Complete absence of the pancreas, curiously, does not always result in unstable diabetes.[4] Furthermore, most juvenile diabetic patients have unmeasurable endogenous insulin secretion without being brittle. Therefore, one cannot conclude that the absence of insulin is the sole cause of diabetic instability.

Several other hormonal abnormalities have been described in brittle diabetes. Circulating immunoreactive glucagon levels are inappropriately high and are not normally suppressed by hyperglycemia or stimulated by insulin-induced hypoglycemia.[5] Growth hormone is also inappropriately high and is not suppressible by hyperglycemia but is excessively stimulated on mild exercise or by rapid decreases in blood glucose levels even if hypoglycemia does not occur.[6,7] Sympathetic overactivity via alpha receptors may contribute to hypersecretion of growth hormone in juvenile diabetic patients.[8] None of these findings are found exclusively in unstable diabetes, and none explains the instability. The cause or causes of instability remain unknown. The increased levels of glucagon and growth hormone are probably secondary manifestations.

Juvenile Diabetes

The diagnosis of diabetes in the child usually follows abrupt onset of polyuria and polydipsia. A glucose tolerance test is unnecessary when glycosuria is present and fasting blood sugar levels are in excess of 130 mg/dl. Treatment is initiated for ketoacidosis if indicated, or with insulin and diet if ketoacidosis is absent.

The juvenile diabetic patient can be expected to become more unstable, both emotionally and in respect to control of diabetes, at the onset of adolescence. Apparently unstable diabetic patients often become stable if the usual therapeutic errors are avoided (Table 1). A check also should be made for coexisting conditions that may affect diabetes (Table 2). The commonest cause of instability in large referral centers for juvenile diabetic patients is overdosage of insulin.[2] More lenient standards of control must be used for the juvenile diabetic patient than for the adult with stable diabetes. A reasonable goal for the adult with stable diabetes is normal blood glucose levels at all times. Such a goal is attempted in juvenile

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TABLE 1
Therapeutic Errors Associated with Unstable Diabetes

Irregular pattern of food ingestion, exercise, and insulin injection
Faulty testing for urinary glucose and ketones
Wrong estimate of duration of insulin action
Abuse of drugs: steroids, diuretics, adrenergic blockers
Abuse of alcohol, carbohydrates

TABLE 2
Coexisting Conditions Affecting Stability of Diabetes

- Incomplete bladder emptying
- High or low renal threshold for glucose
- Unrecognized endocrine disturbance
    - Hyperthyroidism
    - Adrenal or pituitary failure
    - Menstrual cycle
    - Pregnancy, parturition
- Psychologic factors
- Systemic disease: trauma, infection, renal failure, hemodialysis

diabetes, but is obtainable in only a small percentage of juvenile diabetic patients because their blood sugar levels are inherently more variable. Although most adults with diabetes can achieve a 24-hour urinary glucose excretion of less than 10 g/day, such a goal in the juvenile with unstable diabetes often results in catastrophic hypoglycemic reactions from an overdosage of insulin. A more reasonable goal for the juvenile is less than 20 g. of urinary glucose per 24 hours, but some authorities believe that good control is achieved in the juvenile when urinary glucose levels are between 20 and 60 g/24 h.[9]

Diet Therapy

Certain aspects of dietary instruction are particularly important in unstable diabetes: (1) the regularity of food intake, both in quantity and timing, (2) the provision of midmeal and bedtime snacks, and (3) the need for additional snacks to cover unexpected exercise. Currently there is less rigidity about carbohydrate restriction, the use of weighed diet, and the use of exchange lists. The consensus concerning juvenile diabetes is that good control without creating excessive psychologic conflicts is a desirable goal and that good control of blood glucose cannot be achieved without some dietary control.[10] The debate over free-versus-controlled diets in juvenile diabetes cannot be resolved yet because of the lack of reliable data. Knowles found that the prevalence of degenerative complications were similar in two groups of juvenile diabetic patients regardless of whether free or restricted diets were used.[11] Others, however, have found significantly less chronic complications with the use of controlled diets.[12,13]

The constancy of quantity and timing of food intake is important because the fuel must be closely matched to the insulin supply. The ideal duplication of normal human physiology would require the supply of insulin into the portal vein in short bursts after food ingestion. This will probably never be a therapeutic possibility except under costly and limited research circumstances employing pancreas transplantation or computerized injection equipment. We therefore should provide the patient with the best compromise available, that is insulin given parenterally so that peak insulin levels coincide with peak glucose levels.

Urine Testing

The qualitative testing of a second voided urine sample is performed by the patient before each meal and at bedtime. The results are recorded in a log booklet in which the patient also should indicate any unusual developments, such as insulin reactions, intercurrent illnesses, and polyuria, and the insulin dosage for each day. We have found that the patient becomes more enthusiastic about self-care of diabetes if this record is attentively reviewed by the physician at each office visit. The patient with unstable diabetes requires review by the physician or trained paramedical diabetes worker every one or two months. If the urine is strongly positive for sugar for one or two days, the urine should be tested for the presence of acetone. The juvenile patient and parent soon learn that a positive acetone test reaction does not always portend hospitalization for ketoacidosis, especially when glucosuria is mild. Mild acetonuria is common after overnight fasting, during exercise, or during mild illnesses.

The use of quantitative urine glucose tests can be applied to fractions of a 24-hour period. A convenient schedule calls for the patient to collect all urine from 8:00 a.m. to noon, noon to 5:00 p.m., 5:00 p.m. to 10:00 p.m., and 10:00 p.m. to 8:00 a.m. The quantity of glucose in each of these samples is a much more useful guide for the fine adjustment of the insulin dose than is qualitative testing of spot urine samples, which cannot distinguish among concentrations of urine glucose that are 2% or more. Fractional quantitative testing may be a more satisfactory method of monitoring some unstable diabetic patients than qualitative testing, and can be carried out inexpensively every two or three months.[9]

Insulin Treatment

Data to support the use of one insulin administration technique over another are limited. The following guidelines may be useful. Initiate insulin therapy in the simplest way possible—a single injection of long-acting NPH or lente insulin before breakfast. Second, split the dose of long-acting insulin if the total exceeds 60 to 70 units per day. Usually two-thirds of the dose is given before breakfast and one-third before supper. Third, if a single or split dose of long-acting insulin is ineffective in controlling glycosuria, as usually occurs in unstable diabetes, supplements of short-acting insulin (regular or semilente) are added to the program. Fourth, the patient is told to make adjustments in insulin dose and timing no oftener than every two or three days. Table 3 lists some general or average characteristics of different insulins. There is considerable individual variation in the onset and duration of insulin action. The ability of a child to give his own insulin must be assessed individually. Fifth, an ampule of glucagon (1 mg) should be available for someone close to the patient, who is instructed in the method of administering it parenterally if the patient suffers a severe hypoglycemic reaction or is unable to take a sugar solution orally.

Management depends much on how knowledgeable and reliable the juvenile patient or parent is in adjustment of insulin. The unstable diabetic patient who is careless cannot achieve good control of his conditon without fundamental changes in behavior. However, even the careful, fully informed patient may not be able to achieve good control of his diabetes.

The more unstable the diabetes, the more one should rely on the value of the 24-hour urinary glucose for guidance in insulin dosage. This test can be taught to a parent and can be used for periodic monitoring in the home. A 24-hour urine collection is tested with Clinitest tablets. A 4+ reaction requires dilution of the urine until 2 or 3+ results occur.

Litman[10] advised that the juvenile diabetic patient strive for a fasting blood sugar level that is between 150 and 250 mg/dl, a 24-hour urine glucose value between 15 and 25 g, normal growth and absence of insulin reactions and ketosis. The first priority in managing the brittle diabetic patient is to eliminate insulin reactions because they: (1) are potentially harmful to health, and (2) create instability of diabetes because of the Somogyi effect. The second priority is to avoid ketosis. The management of a juvenile diabetic patient who is less than three years old is less rigid than for older children.

TABLE 3
Some Characteristics of Different Insulins

Insulin	Physical Characteristics	pH	Source	Ingredients (mg/100 units) Protein	Zinc	Buffer
Regular	Clear	7.2	Beef, pork, mixed	0	0.03	0
Semi-lente	Suspension	7.2	Beef	0	0.2	Na acetate
NPH (Isophane)	Suspension	7.2	Beef, pork	0.4-0.5	0.3	Na phosphate
Lente	30% semi-lente 70% ultra-lente	7.2	Beef, pork, mixed	0	0.2	Na acetate

Ultralente and PZI insulin are no longer used by most clinics for treatment of unstable diabetes.[14] Oral agents have no place in the management of the unstable diabetic patient, who is presumed to have no capacity to secrete endogenous insulin. The use of adrenergic blocking drugs (for example, propranolol) to stabilize the control of diabetes cannot be recommended for general use. The drug has been advocated in the control of marked emotional changes in preadolescent diabetic girls.[15] Beta-adrenergic blocking drugs reduce the ability of the liver to release glucose during hypoglycemic reactions, and therefore may aggravate insulin reactions.

Following are questions frequently asked by unstable diabetic patients. In many instances, these questions and answers also apply to the stable diabetic patient.

Q: If I plan to play in a sport, what do I do about my meals and insulin that day?

A: It is simplest to have an extra snack just before the extra activity. If insulin reactions still occur, it will be necessary to decrease the insulin dose as well.

Q: How much should I reduce the insulin dose if, for example, I want to play basketball?

A. This cannot be answered the same way for every patient. Ask your doctor's advice. The morning insulin dose may need no change at all, or it may need to be lowered by 20 to 50% before vigorous activity.

Q: What is the point of being fussy about my urine sugar if I'm going to get blind and go into kidney failure later on anyway?

A: No one can guarantee freedom from vascular complications by keeping blood and urine sugar levels well regulated. What one can guarantee is the elimination of insulin reactions and ketoacidosis and the expense and danger that go with them. We also have increasing evidence that complications such as blindness and kidney failure can be delayed, if not prevented, by improved control of hyperglycemia.[16]

Q: What changes should we make in our child's care when he is sick with the flu?

A: During most acute viral illnesses, the diabetic patient needs as much or more insulin than when he is well. So maintain the insulin dose and give additional short-acting insulin if needed, even if vomiting occurs. Maintain hydration with calorie-containing fluids, such as juices.

Q: Do emotional upsets throw the diabetic patient out of control?

A: Yes, but this is an unusual cause of instability.

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Continuing Medical Education

Minnesota Obstetrical and Gynecological Society

Annual Meeting of The Minnesota Obstetrical and Gynecological Society, Saturday, December 4, 1976. Health Sciences "A" Building of the University of Minnesota Hospitals, Minneapolis. Guest speaker will be Warren Pearce, M.D. President, Dr. Loren Jacobson; Vice President, Dr. John M. Brown; Secretary-Treasurer, Dr. Charles Fish. Contact: C. R. Fish, M.D., Mayo Clinic.

Breast & Gynecologic Malignancies

The Miller-Dwan Medical Center Foundation is sponsoring a seminar November 19-20 at Miller-Dwan Hospital in Duluth on "Breast and Gynecologic Malignancies." The program is offered in cooperation with the Duluth Chapter-American Academy of Family Physicians. Content is approved for 10 hours Category I Credit through the AMA, and application has been made to the AAFP for 10 hours prescribed credit. Registration fee is to be announced. Interested individuals should contact Gene Cotton, M.D., at Miller-Dwan Hospital, Duluth, Minnesota.

Acute Diabetic Complications

BRUCE R. ZIMMERMAN, M.D.*

Diabetic ketoacidosis and the associated conditions of nonketotic hyperosmolar coma and lactic acidosis require prompt recognition and treatment by the physician. This paper reviews the physiological alterations and makes specific recommendations to correct them.

SINCE THE INTRODUCTION of insulin to treat diabetes, and improvements in fluid therapy, the frequency and mortality of diabetic ketoacidosis has diminished. Consequently, the interest of both the researcher and the clinician has focused on the chronic complications of diabetes and the problems of improving daily management. Despite this, all physicians must be able to recognize and initiate treatment in diabetic ketoacidosis and the related disorders of nonketotic hyperosmolar coma and lactic acidosis.

The purpose of this paper is to review the clinical features, pathogenic factors, treatment, and physiologic responses in these disorders. Better understanding of the clinical features and biochemical derangements should improve therapy. In diabetic ketoacidosis, significant reduction in the number of deaths probably can occur only through better patient education.[1]

Clinical Features

Diabetic Ketoacidosis

Diabetic ketoacidosis is reported to occur in three of each 1000 diabetics per year.[2] Effective patient education programs decrease this incidence significantly. Education is unlikely to affect incidence with unknown precipitating factors, with sudden serious illness, or in new cases of diabetes.[3] The diagnosis of diabetic ketoacidosis is not a problem when a careful history, physical examination and simple laboratory studies are obtained.[4-6] When consciousness is impaired, the differential diagnosis usually includes other causes of coma of slow onset such as uremia, drug overdose, cerebral vascular accident, hyperosmolar coma, and, in young children, salicylate intoxication. Similar findings may occur after head injury.[4] "Physiologic ketosis," which occurs with starvation and prolonged exercise, is associated with only a mild hyperketonemia. Total ketone bodies remain below 5 mM/liter without appreciable acid-base disturbance, so this disorder is easily distinguished.[7]

Poorly nourished alcoholic patients who have repeated bouts of vomiting may accumulate sufficient ketones, even in the absence of diabetes, to cause metabolic acidosis. Blood glucose levels are less than 250 mg/dl and urine tests do not show a 4+ reaction for glucose.[8]

Hypoglycemia is rarely difficult to differentiate from ketoacidosis. Urine tests, rapid Dextrostix testing, and even testing of tears can quickly make the distinction in most cases. Intravenous 50% dextrose may be employed as a diagnostic test of hypoglycemia.

The most common precipitating causes of ketoacidosis include infection, mismanagement by the patient or physician, and onset of juvenile diabetes. In about 25% of cases no precipitating cause can be found.[1,5,9] Acidosis is most prevalent in the first five years after diagnosis.[4] Adolescent patients often stop taking insulin for emotional reasons.[5] Other precipitating factors include myocardial infarction, pregnancy, pancreatitis, dialysis, and the effect of thiazides and glucocorticoids.[3] Occasionally there may be a relationship to menstruation.

Usually progression to ketoacidosis takes a day or more.[5] Particularly in the child, the progression is so unpredictable that continuous medical surveillance is recommended once the diagnosis

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of diabetes mellitus is suspected.[4] Respiratory depth and rate both increase once the serum CO_2 is less than 15 mM/liter or the pH is less than 7.25. Vomiting is an ominous symptom as it signals deterioration to severe acidosis. The abdominal pain of ketoacidosis may mimic a surgical emergency. Although often called diabetic coma, impairment of consciousness varies in ketoacidosis and true coma occurs in less than 15% of patients. Decreased skin turgor, softened eyeballs, and dry mucous membranes are signs of dehydration and an acute weight loss of at least 5%. When weight loss approaches 15%, circulatory collapse occurs or is imminent. Hyperlipidemia may be suspected by the presence of lipemia retinalis, eruptive xanthoma, or lactescent serum.

Mortality is less than 10%[1,2,9,10] in adults, and should be almost nonexistent in children. Factors increasing mortality are advanced age, increased urea levels, increased osmolality, hypotension, prolonged coma, high lactic acid levels, low pH, hypokalemia, infection, and myocardial infarction.[1,2] Common causes of death are myocardial infarction, cirrhosis, pneumonia, hypokalemia, aspiration, pancreatitis, and renal failure. In pregnancy, the fetal death rate is over 50%.[1,9] A recent autopsy study indicates disseminated cerebrovascular coagulation is important.[11] Sickle cell anemia crisis has been precipitated by ketoacidosis and has caused death.[12]

Diabetic ketoacidosis is defined by the laboratory findings. Although limits are arbitrary, usually ketones are greater than 7 mM/liter and arterial pH is less than 7.25 or serum bicarbonate is less than 10 mEq/liter.[8] Beta-hydroxybutyric acid and acetoacetic acid are generally present in a ratio of 3:1. Acetone is formed by the spontaneous nonenzymatic decarboxylation of acetoacetate. Although acetone may circulate in amounts up to 12 mM/liter, it doesn't contribute to the lowering of pH.[8] The sodium nitroprusside reagents (Acetest and Ketostix) commonly used for qualitative measurement of ketones are sensitive mainly to acetoacetate, less to acetone, and not at all to beta-hydroxybutyrate.[13] With associated lactic acidosis the proportion of beta-hydroxybutyrate increases, because of complex thermodynamic factors.[13] This can cause an under-estimation of ketones. With impairment of renal tubular function, ketoacidosis may occur without ketouria, making reliance on urine ketones alone hazardous.[14] Hyperglycemia may range from 150 to 2000 mg/dl[4] with a mean about 600 mg/dl. Elevation of plasma glucose is associated with a reciprocal decrease in serum sodium concentration. This decrease can be approximated by assuming a sodium decrease of 1.6 mEq/liter for each 100 mg/dl increase in glucose. Mean fluid deficit is six liters and occurs when the filtered glucose load exceeds the renal tubular reabsorptive capacity, producing osmotic diuresis. Additional solute for excretion is derived from protein catabolism and ketouria, both of which require water and cation loss.[4] Water losses exceed electrolyte losses. The hypertonicity, acidosis, and loss of cellular volume lead to potassium depletion, which usually is not reflected in the initial serum potassium level because intracellular potassium shifts to the extracellular fluid. Magnesium, calcium, chloride, phosphate, and nitrogen are also lost in the urine. Leukocyte counts are elevated, averaging 18,000/mm^3 in one series. This increase does not necessarily indicate infection.[9]

An increase in plasma glucagon has been confirmed in patients with severe diabetic ketoacidosis, and there is a minor statistical correlation between glucagon levels and other measures of the severity.[15] Somatostatin infusion suppresses glucagon increase in insulin-deficient diabetics and, at the same time, slows glucose increase, prevents ketosis, and lessens alanine, free fatty acid, and glycerol increases suggesting that glucagon has an etiologic role in ketoacidosis.[16] Other hormones, such as cortisol, norepinephrine, epinephrine, and growth hormone, are insulin antagonists and may be increased in patients presenting in severe ketoacidosis. Studies of hormonal changes in insulin deprived juvenile diabetics show that these changes are late and probably secondary to the ketosis,[17] not causative of it. Regardless of the clinical and biochemical features, the initiating event in ketoacidosis is a relative or absolute deficiency of insulin which then leads to increased peripheral free fatty acids, hepatic overproduction of glucose and ketones, and limited peripheral utilization of ketones.[18] The altered metabolism results in all the other changes mentioned.

Nonketotic Hyperosmolar Coma

In some patients, glucose overproduction predominates and significant ketosis is absent. There are a number of hypotheses to explain this syndrome.[14] It should be considered part of a continuous spectrum of insulin deficiency, ranging from relatively pure ketoacidosis with minimal fluid loss and complete insulin deficiency, through associated acidosis and dehydration, to marked hyperosmolarity, dehydration, and partial insulin deficiency.[19] If this spectrum is remembered, recognition of and adequate therapy for the patient with a mixed picture should not be difficult.

Nonketonic hyperosmolar coma was first described by Dreshfeld in 1886[14] but has only received general recognition since about 1957. In contrast to ketoacidosis, it usually occurs in the obese, maturity-onset diabetic who has an insidious history that may cover days and even, occasionally, weeks. By definition, ketosis sufficient to produce acidosis is absent. Neurologic changes are frequent, and the most common admitting diagnosis is a cerebrovascular accident. Reported focal neurologic changes have included aphasia, homonymous hemianopsia, hemisensory deficits, hemiparesis, hyperreflexia, positive Babinski signs, visual hallucinations, tonic eye deviation, and autonomic changes manifested by hyperpnea and hypertension.[20-23] Grand mal or focal seizures, which are characteristically repetitive and resistant to anticonvulsant therapy, occur in 10 to 15% of patients. In surviving patients, the neurologic deficit most often resolves promptly without sequelae.[14,20,22] The impairment of consciousness is generally attributed to cerebral intracellular dehydration produced by the increased serum osmolality,[14,19] but this hypothesis is difficult to correlate with the finding that cerebral dehydration is not present at autopsy. The focal signs may be due to previous structural cerebral lesions such as infarctions or hemorrhage[23] associated with atherosclerosis and cerebral anoxia.

Precipitating illnesses include infections, particularly pneumonia, acute pancreatitis, and extensive body burns. Associated drugs include phenytoin, steroids, chlorthalidone, immunosuppressive agents, and diazoxide.[19,21,22,24,25] Associated therapeutic procedures include peritoneal dialysis, hemodialysis, tube feeding of high-protein formulas, high carbohydrate infusion loads, use of mannitol and urea, induced hypothermia, and renal transplantation.[19,21] Some believe that a history of increased carbohydrate intake during the prodrome is common. Renal failure is said to be a necessity for development of the syndrome by some authors.[25] Prognosis is much worse than in ketoacidosis, averaging about 50% mortality. Delay in seeking medical assistance and in diagnosis may be a major cause of the poor prognosis.[9] Gram negative infections appear to be particularly ominous, with the mortality rate approaching 100%.[19]

Despite these general differences, comparisons of age, blood glucose levels, and insulin levels do not provide a clear distinction from ketoacidosis. Arbitrary criteria for the definition of nonketotic hyperosmolar coma are a plasma glucose greater than 600 mg/dl and serum osmolality greater than 350 milliosmoles/kg with serum acetest not greater than 2+ in 1:1 dilution.[25] Osmolality is calculated by the following formula:[2,14,19]

$$\text{Osmolality, mOsm/Liter} = 2(\text{Na} + \text{K}^+)\ \text{mEq/liter} + \frac{\text{glucose mg/dl}}{18} + \frac{\text{urea}}{6}\ \text{or}\ \frac{\text{BUN}}{2.8}$$

Normal is less than 300 mOsm/Liter. If the calculated value is less than 320 mOsm/Liter, the formula tends to overestimate the osmolality and if greater than 330 mOsm/Liter, to underestimate.[10] In two large series, the water deficit was so severe that serum osmolality averaged 384 and 374 mOsm/Liter.[19]

The reasons for reduced ketosis in hyperosmolar coma are not known with certainty. Postulated factors include dehydration, hyperglycemia, decreased free fatty acid concentrations, and direct insulin effects on hepatic ketogenesis.[19,26] None of these is likely to be the full explanation. Peripheral insulin measurements show no significant differences from ketoacidosis, with low values obtained in both. Because of their severe volume depletion and reduced glomerular perfusion, these patients are extremely vulnerable to the development of a secondary lactic acidosis.[14]

Lactic Acidosis

Of the problems discussed in this review, lactic acidosis is the one that is not necessarily associated with a insulin lack and should be considered in any condition producing tissue hypoxia. The differential diagnosis is any metabolic acidosis with an increase in unmeasured anions ar calculated by any of the following formulas:

$$
\begin{aligned}
\text{Normal ``anion gap''} &= 0 \pm 3\ \text{mEq/ml} = (\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-) - (17)\\
\text{OR} &= 8 \pm 4\ \text{mEq/ml} = (\text{N}^+ + \text{K}^+)\text{mEq/l} - (\text{Cl}^- + \text{HCO}_3^-)\\
\text{OR} &= 12\ \text{to}\ 15 = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)
\end{aligned}
$$

Conditions producing such an increase are diabetic ketoacidosis, ketoacidosis associated with alcoholism, salicylate intoxication, methanol poisoning, paraldehyde ingestion, ethylene glycol poisoning, uremia, and lactic acidosis.[27,28] Excess blood lactate is found after exercise and forced breathing but these are not diagnostic problems. It does become important diagnostically in many other cases, including endotoxic or hemorrhagic shock, cardiopulmonary bypass, acute hypoxemia, pulmonary edema, severe anemia, leukemia, ethanol ingestion, use of phenformin, pancreatitis, and acute hepatic failure.[27,29,30]

As could be expected with such diverse etiologies, the clinical features vary widely. Apart from the features of the precipitating illness, hyperpnea should provide a clue to the diagnosis. When compared with diabetic ketoacidosis, in lactic acidosis the hyperpnea is exaggerated. Also seen relatively commonly are shock, bradycardia, anemia, and hypothermia.[30]

Phenformin has several effects which promote the development of lactic acidosis. It inhibits formation of glucose from lactate and pyruvate and both decrease hepatic uptake of the lactate formed and increases hepatic output of lactate.[13] Renal or hepatic failure accelerates these effects so phenformin should never be given to the patient with either renal or hepatic failure.[30] Ethanol intake by the patient further impairs gluconeogenesis from lactate and may accelerate the changes induced by phenformin.

In most areas, the diagnosis of lactic acidosis remains one of exclusion. Where available, the enzymatic measurement of plasma lactate confirms the diagnosis. A plasma lactate of 7mM/Liter or greater is, by definition, diagnostic of lactic acidosis. In more difficult cases, finding an elevated lactate-pyruvate ratio is helpful.[31] As mentioned earlier, the contribution of ketoacidosis to the "anion gap" may be underestimated by the nitroprusside test for ketones because formation of beta-hydroxybutyrate (which is not measured by this reagent) is favored.

Cerebral Edema

This entity is discussed not because it is a presenting problem in the diabetic patient but because its recognition and prevention have played a dominant role in recent debates about the therapy of ketoacidosis even though the incidence is very low.[2,19,32,33]

The common presentation is that of an adolescent who has a good initial response to treatment of ketoacidosis but who then develops progressive mental deterioration despite continued biochemical response. This deterioration may be accompanied by papilledema, dilated or unequal pupils, hyperpyrexia, and, occasionally, diabetes insipidus.[8]

Three separate factors seem to be involved in the development of late cerebral edema. Studies monitoring cerebrospinal fluid pressure have shown that an abnormally high CSF pressure develops when plasma glucose and osmolality fall.[34] Spinal fluid glucose reduction lags behind plasma glucose, causing a transient reversal of the CSF to plasma glucose ratio.[20,32] Contributing to the increased spinal fluid osmolality is the production of osmotically active metabolites such as sorbitol, fructose, and myoinositol which is stimulated by the hyperglycemia.[32,35] An unidentified solute called "idiogenic osmoles" has also been implicated.[20] Interestingly, it is stated that these shifts do not become important as long as plasma glucose remains above 250 mg/dl.[20,35]

Spinal fluid monitoring studies have also shown initial normal or increased spinal fluid pH with a parodoxic fall as blood pH rises.[36,37] As plasma bicarbonate rises in response to treatment, part is converted to CO_2 which easily diffuses into the CSF. In contrast, movement of both HCO_3^- and H^+ is retarded by the blood-brain barrier. As CSF pCO_2 rises faster than bicarbonate, pH falls. It is not commonly appreciated that cells of the whole body exhibit the same differential permeability and will experience the same fall in pH.[35] Despite these changes, neurologic manifestations usually can not be directly correlated.[20]

Finally, cerebral hypoxia may contribute to the cerebral edema. 2,3-Diphosphoglycerate (2,3-DPG) is an organophosphate which binds to deoxyhemoglobin, lowering its affinity for oxygen and facilitating delivery of oxygen to tissues. Low levels of 2,3-DPG have been reported in diabetic ketoacidosis, shifting the oxygen dissociation curve to the left. Acidosis counteracts these effects, shifting the curve back to the right and normalizing oxygen delivery. Correction of the acidosis eliminates this helpful shift back to the right and elevation of 2,3-DPG lags behind, decreasing delivery of oxygen to the tissues.[38-40] Discussion of the relative contribution of each of these mechanisms and proof of their existence is beyond the scope of this review.

Treatment

Successful treatment depends on individualization of therapy, with careful and repeated monitoring of clinical and laboratory data. To accomplish this, a detailed flowsheet showing fluids and insulin administered and the timing and results of blood tests is essential.

Controversy in methods of care extends even to minor points such as bladder catheterization, stomach aspiration, and ECG monitoring. Again individualization is the key. Prudent recommendations are:

1. Catheterization not routinely but reserved for patients with low urine output after initial treatment
2. Gastric aspiration in obtunded patients with repeated vomiting or evidence of gastric dilatation
3. ECG monitoring when potassium is infused at rapid rates, when rapid serum potassium measurements are not available, or when initial serum potassium is abnormal
4. Repetition of blood glucose, electrolyte, and arterial pH measurements in one to two hours and then at intervals of two to four hours depending on response
5. A central venous catheter to monitor fluid replacement in the patient with shock.

Regardless of other therapeutic measures, an important aspect of the initial evaluation and clinical follow-up is a thorough search for the precipitating cause, particularly infection. If infection is identified or strongly suspected, then antibiotics should be started after appropriate cultures are made.

Insulin

Although preceded by a series of studies using increasingly lower doses of intravenous or intramuscular insulin successfully to treat ketoacidosis, not until the publication of three articles together in June 1974[41-43] did continuous low-dose insulin infusion receive widespread editorial[44-46] comment and create a new controversy.[47] Several facets of this treatment method are clearly established. The effectiveness of this method contradicts the concept that acute insulin resistance or hyposensitivity exists in ketoacidosis. The serum half-life of insulin is in the range of three to seven minutes and within 25 minutes after the administration of an intravenous bolus of insulin, the serum levels will be back to basal levels in the diabetic patient without insulin antibodies. Recently a biexponential decay equation with a two compartment open model has been found. The second compartment is comparable to total body water and has a slow half-life of 211 minutes.[48] Using these figures, it can be calculated that a priming dose of 0.2 U/kg followed by a constant infusion of 0.05 U/kg per hour results in a steady-state serum insulin concentration of about 130 μU/ml.[48] Maximal glucose transport occurs at serum insulin concentrations of less than 200 μU/ml.[42,45] Constant insulin infusion can be adjusted easily to achieve constant serum insulin levels in this range, avoiding the vagaries of absorption from tissue depots and overcoming the problem of the short half-life of intravenous bolus insulin. Higher insulin doses may be ineffective because of saturation of insulin receptors. Intramuscular insulin has a peak onset and duration of action intermediate between intravenous bolus and subcutaneous insulin[49] and, in similar low doses, has also been demonstrated to achieve an effective serum insulin concentration.[50]

Advantages of constant low-dose infusion are simplicity of administration and control, avoidance of precipitous fall in blood sugar, low risk of hypoglycemia, and low incidence of hypokalemia.[41-43,46,49,51,52]

The major disagreement with the use of low insulin doses is that, in some patients, acidosis deteriorates in spite of correction of hyperglycemia and the gap between correction of the blood sugar and correction of the acidosis is longer.[10] Effective peripheral insulin levels do not necessarily indicate that hepatic levels are high enough to reverse the accelerated hepatic gluconeogenic and ketogenic process.[47] Although initial potassium replacement is identical and initial hypokalemia may be less, urinary potassium losses are greater and late hypokalemia may be a problem.[10] Particularly in the restless patient, constant infusion requires careful nursing attention to prevent unrecognized discontinuation. The rare patient wtih true insulin resistance will present a problem of recognition with either high-dose or low-dose insulin programs. In using low-dose insulin, the relative resistance reported in the early response to insulin in patients with infection[49] should be kept in mind.

Regardless of the method used, the physician must be prepared to modify the insulin dose depending on clinical and laboratory response. Insulin must be continued until ketogenesis has abated and should not be stopped because of blood glucose response.

Reasonable recommendations for each method are as follows:

A. High Dose:
   1. Initial insulin in an average dose of 100 units regular insulin but ranging from 50 to 200 units depending on body size, severity and estimate of insulin antibody status; usually given 50% intravenously and 50% subcutaneously but all intravenously if there is any indication of shock
   2. If the insulin was given all intravenously, then repeat insulin each hour (about 50 units regular insulin) until the blood glucose has fallen to 250 mg/dl; with subcutaneous insulin, repeat injection about every two hours
   3. Further insulin doses as determined by blood glucose levels with a switch to depot insulin on recovery when the patient can resume normal food intake

B. Low Dose:
   1. An intravenous bolus loading dose of 0.1 units/kg body weight of regular insulin.
   2. Continuous regular insulin infusion at a rate of 0.1 units/kg per hour. The insulin can be mixed in a variety of ways. Some suggestions are:
      (a) 100 ml of 0.9% saline and 1 ml U-100 regular insulin to give a concentration of 1 unit/ml. Infuse with an intravenous syringe pump at the calculated dosage
      (b) 500 ml of 0.9% saline and 50 units regular insulin to give a concentration of 1 unit/10 ml. Infuse by a pediatric microdrip at the calculated area
      (c) With either method "wash out" the entire infusion apparatus with the solution before patient infusion.
      (d) At these concentrations, available evidence suggests the common recommendation to add albumin to prevent insulin binding is unnecessary.[41,53] If unconvinced by this data, add 0.5 gm human albumin per 100 ml of solution before adding the insulin.
      (e) Although the insulin solution can be infused "piggy-back" with the other fluids, caution suggests a separate intravenous site
   3. When the plasma glucose falls below 250 mg/dl, decrease the infusion rate to one to five units/hr depending on the rapidity of the fall
   4. When both ketosis and hyperglycemia are corrected and the patient can resume normal food intake, switch to depot insulin

C. Intramuscular Insulin:
   This method seems to have some of the disadvantages of each of the other methods and is probably not preferable to either.

Insulin: Modification for Nonketotic Hyperosmolar Coma. Low-dose constant insulin infusion would seem to be ideal for treatment of nonketotic hyperosmolar coma. Included in several of the series of patients treated for ketoacidosis by this method are a few patients with hyperosmolar coma. If the physician chooses to use this method, he must monitor the patient closely and document the results.

It is often written that hyperosmolar patients are more sensitive to insulin. Some patients are indeed very insulin-sensitive but, on the average, insulin requirements are the same or only slightly less than in ketoacidosis.[19] Use of similar insulin schedules with a tendency to lower doses seems warranted.

Insulin: Requirements in Lactic Acidosis. Lack of insulin is not a primary problem in lactic acidosis but an occasional patient has moderate ketosis and some patients with ketoacidosis or hyperosmolar coma have associated lactic acidosis. In these cases, insulin treatment is useful. If the plasma glucose is less than 250 mg/dl, then intravenous glucose should be given conjointly.[13,54]

Fluids

In ketoacidosis the average body water deficit is 6 liters, the sodium deficit is greater than 7 mEq/kg body weight, and the potassium deficit is greater than 5 mEq/kg body weight.[55]

The major disagreement in current fluid therapy is whether optimal initial replacement is with hypotonic or isotonic saline.[4,8,18,55] Even though hyperosmolality is present, if vascular collapse exists initially, it is best to use isotonic saline to achieve rapid vascular reexpansion. Rarely is it necessary to use plasma. Overall fluid treatment should follow these guidelines, with modifications depending on follow-up electrolyte determinations, urine output, and clinical status:

1. If vascular collapse is present, give isotonic saline, 1 liter or more in the first hour
2. If shock is not a concern, then give 0.45% saline, 1 liter in the first hour
3. Once urine flow is established and blood pressure is stabilized, give 0.45% saline at a rate of 300 to 500 ml/hr.
4. After plasma glucose decreases to 250 mg/dl or after 4 to 6 hours of treatment, switch to 5% dextrose to prevent hypoglycemia and to reduce the likelihood of cerebral edema which may accompany reductions in plasma glucose below 250 mg/dl.[8,18]
5. Once the patient is alert and has normal bowel sounds without nausea, oral fluids may be used
6. Fructose solutions offer no advantages; in some cases they may lead to accumulation of lactic acid through metabolism to pyruvate.[56]

Fluids: Modifications for Nonketotic Hyperosmolar Coma.—In hyperosmolar coma, free-water deficit is even greater and isotonic saline is only indicated in severe vascular collapse. Hypotonic 0.45% saline is the initial fluid of choice but the switch to 5% dextrose can be made early.[14,19] Cardiac status is more apt to be compromised, so the saline load must be carefully monitored. If possible, the oral route is often preferable for fluid replacement.

Fluids: Modifications for Lactic Acidosis. Lactic acidosis may have unique fluid problems which will be discussed separately later.

Potassium

Potassium replacement is similar in all three conditions. The initial serum potassium usually does not reflect the total body potassium because the serum level is low in only about 4% of patients.[57] During treatment, particularly with the use of bicarbonate, serum potassium may drop abruptly.[18] The realization that hypokalemia develops early has led to much earlier institution of potassium replacement than previously.[57] Although rapid laboratory measurements have made it less necessary, the electrocardiogram remains helpful.[1] Initial hypokalemia can be identified by flat or inverted T-waves with ST segment depression. During potassium infusion, development of peaked T-waves and low R-waves indicates too rapid an infusion. Caution must be used in interpreting the changes because ischemic heart disease or digitalis treatment can invalidate them.[58] Considering the dangers of hypokalemia the following recommendations are made:

1. If the initial serum potassium is low or low normal, begin potassium replacement with the initial fluids[18]
2. If the initial serum potassium is high begin potassium replacement when it falls below 4.5 mEq/liter[43]
3. If bicarbonate is used, be particularly alert for hypokalemia[57]
4. Usually administer potassium at a concentration of 40 mEq/liter of fluid
5. A poor urine output is not a contraindication to potassium administration, but caution is necessary if oliguria persists[34]
6. Repletion of red cell 2,3-DPG levels may be facilitated by administering parenteral phosphate, which can easily be given as potassium phosphate[8]

Bicarbonate

With insulin treatment the ketone bodies are oxidized to CO_2 and water, regenerating bicarbonate and correcting the acidosis. This takes time, and severe acidosis increases the risk of cardiac arrhythmia and impairs cardiac contractility. On the other hand, rapid correction of the acidosis may cause the changes mentioned in discussing cerebral edema.[18] In spite of these considerations, the greater danger seems to be withholding bicarbonate from patients in critical need of rapid partial correction of a potentially lethal degree of acidosis.[35] Various formulas exist to calculate the base deficit.[2,6,35,39] None of them is very helpful because the full deficit should not be corrected. Hyperventilation continues in patients who have ketoacidosis in spite of a rise in serum bicarbonate,[35] allowing small increments in bicarbonate to have a striking effect on pH. For the same reason, excessive treatment with bicarbonate can cause post-treatment respiratory alkalosis.[6] Considering these factors the following is recommended:

1. Restrict bicarbonate use to severe metabolic acidosis with pH less than 7.1 or bicarbonate less than 10 mEq/liter

2. Give 100 mEq sodium bicarbonate (or with the older ampules, 88 mEq) added to hypotonic saline
3. With more severe acidosis and pH less than 7.0 give 132 to 150 mEq sodium bicarbonate by intravenous push or added to hypotonic saline
4. Give additional bicarbonate if the pH remains below 7.2 at two hours
5. Lactate was initially introduced because sodium bicarbonate was difficult to sterilize by autoclaving; it is no longer indicated[60]
6. Alkaline solutions are unnecessary in hyperosmolar coma unless there is severe associated lactic acidosis

Lactic Acidosis: Special Considerations

The major thrust of therapy in lactic acidosis is eliminating the primary cause. In some cases, such as severe pulmonary edema, the lactic acidosis subsides rapidly with treatment of the primary cause and without specific treatment for the acidosis.[28] In other cases, very large amounts of bicarbonate, up to 700 mEq, may be required just to maintain a stable pH.[6] Because of this lack of predictability of therapy with alkali, simple calculations are not helpful and biochemical response must be monitored frequently. Early administration of furosemide often helps to initiate urine output and prevent volume overload.[13,30] If the sodium and fluid load still is not tolerated because of cardiac or renal failure, dialysis should be undertaken without delay.[6,27] Sodium acetate has been used in peritoneal dialysis[61] but the advantages are unproven. Methylene blue has also proved to be of limited use.[27]

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Diabetes Mellitus—Cotton (page 788)

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Renal Transplantation in the Diabetic

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One hundred thirty-two diabetic patients with renal failure have been transplanted at the University of Minnesota. Sixty-seven percent of these patients are currently alive, and 61 percent have functioning kidneys.

According to the report of the National Commission on Diabetes, diabetic glomerulosclerosis is the primary cause of death in approximately half of the patients with juvenile onset diabetes.[1] Even though patients with diabetes constitute a considerable portion of the end stage renal failure population, there has been a general reluctance to transplant diabetics at most centers. However, the survival of diabetic patients treated with hemodialysis is poor,[2-4] and dialysis does not offer a satisfactory alternative. Therefore, the University of Minnesota has routinely accepted patients with diabetic nephropathy for renal transplantation since 1969. Our experience with transplantation in a single large series of patients with juvenile onset diabetes is the basis of this report.

Patient Population

Through December 31, 1975, 132 diabetic patients received renal transplants. Seven patients received a second transplant. The characteristics of these patients is summarized in Table 1. Ninety-six patients received kidneys from a living related donor; 30 of the kidneys transplanted to related recipients were from HLA phenotypically identical siblings. Thirty-six patients received grafts from cadaver donors; in 18 instances the donor and recipient shared two or more of four possible HLA antigens, while the remainder were less well matched.

One hundred eleven patients required hemodialysis prior to transplantation; 21 patients were transplanted before dialysis was actually necessary. Early in our experience with diabetics, we observed that visual acuity severely deteriorated during the late stages of uremia, but appeared to stabilize following transplantation.[5] Once serum creatinine reaches a level of 5.0-6.0 mg/100 ml, uremia and hypertension progresses rapidly in the diabetic patient.[5,6] Therefore, we now transplant the uremic diabetic earlier in an attempt to preserve vision.

Eighty-four patients underwent pretransplant bilateral nephrectomy and splenectomy, while 48 patients were treated with a one stage splenectomy-transplant. Because bilateral nephrectomy and splenectomy are a high risk procedure in the diabetic patient,[7] we now perform that operation only in diabetics with severe hypertension (not controlled by medication and optimal dialysis), urinary tract infections, ureteral reflux, or massive proteinuria. Otherwise, pretransplant prep-

TABLE 1
Patient Population Diabetic Transplant Recipients*
University of Minnesota 1969-1975

	Range	Mean
Age	20-59 years	34 years
Duration of Diabetes	7-34 years	20 years
Creatinine at Time of Dialysis or Transplantation	4.3-24 mg/100 ml	11.4 mg/100 ml
Interval from Dialysis to Transplantation	0-26 months	2.5 months

*Men 85 Women 47 Total 132

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aration and posttransplant management is similar to that described for the nondiabetic patient.[8,9]

Results

Patient Survival

Eighty-eight of the 132 diabetic patients are currently alive (67%) and 81 have functioning primary grafts (61%). Figure 1 shows cumulative patient survival, calculated according to the method of Merrell and Shulman,[10] as a function of HLA matching for diabetic recipients of living related and cadaver kidneys. Comparison is made to the combined survival of diabetic patients treated with chronic hemodialysis at two major treatment centers.[2,11] Diabetic recipients of HLA phenotypically identical kidneys survive better than recipients of nonidentical related kidneys. For recipients of cadaver kidneys, HLA matching does not appear to influence patient survival. The combined survival for diabetic recipients of cadaver kidneys is less than that of diabetics receiving identical or nonidentical related kidneys. However, diabetic patients receiving either living related or cadaver kidneys at our institution have a better survival than diabetic patients treated with chronic hemodialysis elsewhere. Only 24% of the diabetic dialysis patients survived two years. In contrast, the survival at two years for all diabetic recipients of living related kidneys is 71% and for recipients of cadaver grafts is 63%.

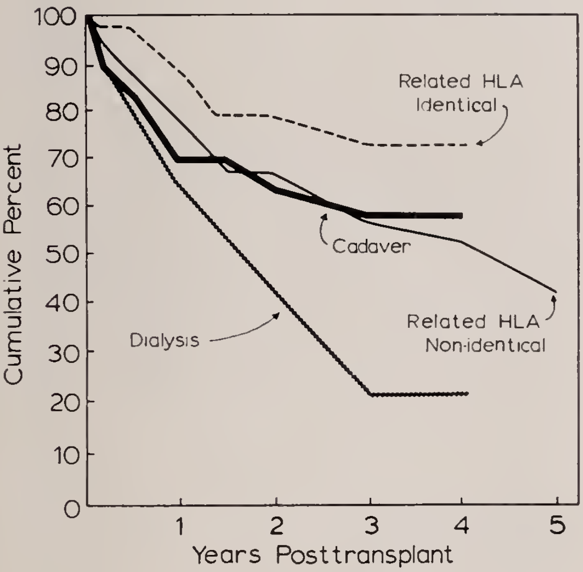

Fig. 1—Cumulative survival of diabetic recipients of related and cadaver grafts as a function of HLA matching with the donor. Comparison is made to the survival of diabetic patients treated with chronic hemodialysis.

Survival of diabetic transplant recipients can be compared to that of 420 nondiabetic recipients (247 related and 173 cadaver grafts) transplanted over the same period of time at our institution. For recipients of related kidneys, cumulative survival for nondiabetic patients is approximately 10% better at one year and 15-20% better thereafter. For recipients of cadaver grafts, cumulative survival for nondiabetic recipients is approximately 12% better at one year. This difference between diabetic and nondiabetic patients persists for subsequent years.

Survival is no different for diabetic men and women recipients. Age does influence survival. Thirty-one of 40 diabetic patients less than 30 years old are alive (78%). Forty-four of 63 diabetic patients between 30-40 years old are alive (70%). However, of those over 40 years of age, only 13 of 29 are alive (45%).

Early transplantation may increase patient survival. Of those diabetic patients not dialyzed before transplantation, six of seven recipients of cadaver grafts (85%) and 10 of 14 recipients of living related grafts (71%) are alive. Whether or not the patient underwent a pretransplant bilateral nephrectomy and splenectomy did not seem to influence survival for recipients of cadaver grafts, but cumulative survival was increased in recipients of living related kidneys who had the pretransplant procedure (86% alive at one year) when compared to those undergoing a one stage splenectomy transplant (73% alive at one year).

Retransplantation has not been very successful in diabetic patients. Only two of seven diabetics who received second kidney grafts after loss of a first graft are currently alive.

Kidney Survival and Function

Figure 2 compares the survival of kidneys in diabetic and nondiabetic recipients of living related and cadaver kidneys. For grafts from living related donors, kidney survival is approximately 8% better in nondiabetic than in diabetic recipients. By two years, grafts in nondiabetic recipients have a 15% better survival, and this difference persists for subsequent years. For cadaver grafts, the difference in kidney survival is less obvious until three years after transplantation. At that time, graft survival is approximately 7% better in nondiabetic than in diabetic recipients, and by four years the difference is 14%. The differences in kidney survival are less than are the differences in patient survival between diabetic and nondiabetic recipients because many more nondiabetic patients survive loss of a primary graft and are alive either on dialysis or following a second kidney transplant.

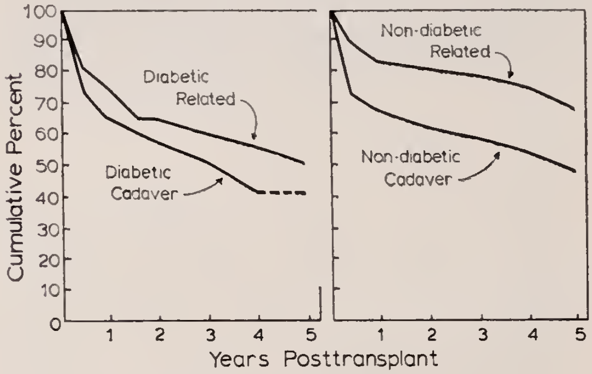

Fig. 2—Cumulative kidney functional survival in diabetic and nondiabetic transplant recipients.

Table 2 summarizes the renal function and blood pressure in the 81 diabetic recipients with primary grafts currently functioning. Renal function is apparently not adversely affected by diabetes during the first few years after transplantation. The excellent renal function parallels the decrease in severity and frequency of hypertension that characterized the pretransplant state of the uremic diabetic.

TABLE 2
Renal Function and Blood Pressure in Diabetic Recipients Surviving with Primary Grafts

	Range	Mean
Creatinine (mg/100 ml)	0.4 — 2.6	1.3 ± 0.4
BUN (mg/100 ml)	8 — 93	25 ± 12
Blood Pressure*	$\frac{88}{54} - \frac{190}{110}$	$\frac{127}{80} \pm \frac{23}{12}$

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*51/81 patients on anti-hypertensive medication

Causes of Kidney Loss

Table 3 summarizes the major causes of 51 graft losses in the diabetic recipients. Almost one-half of those lost were functioning until death of the patient from disorders not related to graft malfunction. Approximately one-third of the kidneys that failed did so because of rejection. Technical complications accounted for the remaining kidney losses. These complications were primarily vascular, urologic, or wound related.

TABLE 3
Cause of Kidney Loss in 132 Diabetic Transplant Recipients

	Number of Losses	Percent of Losses
Death*	24	47%
Rejection	18	35%
Technical	9	18%
TOTAL	51	100%

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*Kidneys functioning at the time of death.

Causes of Death

Table 4 lists the cause of death in the diabetic recipients. Sepsis and cardiovascular disease account for the majority of the deaths. Twenty patients died after loss of the primary kidney graft, six without ever returning to dialysis, three with a functioning second graft, and eleven while on dialysis. In eight of the latter, death was related to complications of dialysis.

TABLE 4
Cause of 44 Deaths in 132 Diabetic Transplant Recipients*

	Number of Deaths	Percent of Deaths
Cardiovascular	12	27%
Sepsis	21	48%
Dialysis Related	8	18%
Other	3	7%
Total	44	100%

Cardiovascular Disease After Transplantation

Table 5 summarizes the occurrence of vascular complications in the diabetic patients. Of the 14 myocardial infarcts, only five occurred in 68 patients with pretransplant evidence of coronary artery disease (any EKG abnormality or history of chest pain), while nine occurred in the 64 patients without pretransplant evidence of coronary artery disease. Peripheral vascular disease is a common problem in the diabetic transplant recipients. Twenty-seven patients required 32 amputations. Finger amputations were primarily related to ischemia secondary to arterial venous fistulas or prosthetic shunts for dialysis, either constructed before transplantation or after loss of a graft necessitating return to dialysis. Seven of the 12 patients with leg amputations are currently alive.

TABLE 5
Cardiovascular Disease Following Transplantation in 132 Diabetic Patients

	Number	Incidence
Myocardial Infarcts		
Fatal	6	4.6%
Non-Fatal	8	6.0%
Cerebral Vascular Accidents		
Fatal	2	1.5%
Non-Fatal	2	1.5%
Peripheral Vascular Disease Requiring Amputation		
Finger	11	8.3%
Toe	9	6.8%
Leg	12	9.1%
Total Number of Patients*	40	30.3%

*10 Patients are in 2 or more groups.

Vision After Transplantation

Table 6 summarizes visual acuity changes during the first year in 89 eyes examined serially before and after transplantation in 55 diabetic patients. In eyes with good vision (better than 20/40) at the time of transplantation, little change in vision occurred during the first year. By two years only 14% had deteriorated and by three years only 20% had deteriorated. For eyes with poor vision, progressive deterioration is more likely to occur, although some eyes may improve or stabilize.

Neuropathy After Transplantation

Most patients have electromyographic and clinical evidence of neuropathy at the time of transplantation. Nerve conduction defects, measured electromyographically, do not improve following transplantation,[12] but clinical improvement is striking. Before transplantation, 22 of 132 patients (17%) had such severe muscle weakness that they were either confined to bed or a wheelchair or could walk with assistance only. After transplantation, 16 of these patients had improvement in muscle strength and ability to walk. Only five patients have had progression of neuropathy and increased difficulty with walking after a successful transplantation. Of the 74 diabetic patients currently alive who have not had leg amputations, only three (4%) have neuropathy severe enough to seriously restrict mobility.

Recurrence of Disease

Light and immunofluorescent microscopic examination of kidney biopsy specimens obtained from our diabetic patients has been carried out by Mauer et al.[13,14] Ten of 12 kidneys biopsied more than two years after transplantation showed hyaline refractile material in afferent and efferent glomerular arterioles. These deposits were not seen in kidneys examined from nondiabetic recipients. In addition, linear staining for IgG and albumin on tubular basement membrane and Bowman's capsule occurred with greater frequency and intensity in kidneys transplanted to diabetic patients.

These lesions are morphologic only and do not presently affect renal function. Mean serum creatinine level was 1.6 mg/100 ml in the diabetic patients from whom the biopsy material was obtained. No functional recurrence of diabetic nephropathy has been observed in the diabetic recipients followed to date.

Rehabilitation After Transplantation

Vocational rehabilitation in our diabetic patients has been assessed by Haymond et al.[15] Of the 88 patients alive, 65 (74%) are either employed, in school, avocationally active, or work at home. Five patients (6%) are unemployed, and 18 patients (20%) are unable to work or be active because of visual, vascular or neurological complications or dependence upon dialysis after loss of the kidney. However, these handicaps can be overcome because some of the rehabilitated patients also have one or more of these disabilities. Approximately an equal number of males and females are active. Forty-three percent of males are employed full or part time and 30% are avocationally active or are students. Eighteen percent of females are employed, and 58% are avocationally active or are active as homemakers.

Discussion

From our own experience,[16-18] kidney trans-

TABLE 6
Visual Acuity Changes in Diabetic Renal Transplant Patients One Year after Transplantation

Vision time of Transplantation	Eyes at Risk	Percent Stable	Percent Deteriorated	Percent Improved
>20/40	46	96%	4%	—
20/40-20/200	12	33%	33%	33%
<20/200	31	26%	58%	16%

plantation is the treatment of choice for the diabetic patient with end stage renal failure. Although the survival of diabetic patients is not as good as that of nondiabetic patients following transplantation, it is clearly superior to that achieved on dialysis. In addition, the social and psychological well being of most diabetic patients is improved following transplantation.[19]

The uremic patient with diabetic nephropathy should be transplanted at an earlier stage than the patient with uremia from other causes. Delaying transplantation allows uremia and hypertension to aggravate diabetic retinopathy.[5] Fluid overload is particularly difficult to manage in the uremic diabetic.[4] In addition, vascular access is a serious problem in the diabetic who must be dialyzed.[4,20] For those reasons, we urge early referral of uremic diabetics to a renal treatment center with transplant capabilities.

Related donors should be used whenever possible. Diabetic patients receiving kidneys from HLA phenotypically identical sibling donors have better survival than those receiving kidneys from nonidentical related donors. Similar observations have been made in our nondiabetic recipients of related grafts.[21] Although diabetic recipients of cadaver kidneys sharing two or more antigens with the donor did not survive better than those less well matched, the reverse is true in our nondiabetic population.[22] The number of diabetic recipients of cadaver grafts is small, and more must be transplanted to determine the influence of HLA matching in this group.

Only small series of transplants in diabetics have been reported from other institutions.[23,24] In general, their experience is similar to ours. The American College of Surgeons/National Institutes of Health Organ Transplant Registry has excluded the University of Minnesota in a recent report summarizing patient and kidney survival in diabetic recipients transplanted at other institutions reporting to the Registry.[25] According to the Registry, approximately 74% of diabetic recipients of related grafts are alive at three years, and 57% have functioning kidneys. For diabetic recipients of cadaver grafts, 57% are alive at three years but only 26% have functioning kidneys at that time. Patient survival for recipients of either related or cadaver grafts transplanted elsewhere is similar to that achieved at the University of Minnesota. However, functional survival of kidney grafts transplanted elsewhere is much less than at our own institution. The use of antilymphoblast globulin for immunosuppression may be responsible for the increased survival of cadaver kidneys at the University of Minnesota.[26]

Although transplantation is beneficial for most diabetics with end stage renal failure, many continue to have significant problems following transplantation. Technical complications of transplantation are more frequent in the diabetic.[27] Cardiovascular disease following transplantation is many fold higher than in our nondiabetic recipients. Septic complications are also more frequent. In addition, diabetic patients tolerate loss of the grafted kidney less well.

The diabetic recipient also presents special problems in management. For example, hyperglycemia itself can elevate serum creatinine, producing a syndrome mimicking rejection.[28] In addition, exogenous insulin requirements may increase considerably following transplantation, probably because of the effect of steroids and the presence of a kidney able to metabolize insulin.[16]

Although significant problems do exist following transplantation in the diabetic, they probably are less severe than those associated with dialysis.[4] In addition, real benefits occur after successful transplantation. The clinical improvement in neuropathy is particularly striking. In addition, stabilization of vision is most important. The blind diabetic is at a severe disadvantage, and any measure to preserve vision is worthwhile. Congestive heart failure may also be relieved following transplantation. Vocational rehabilitation is almost impossible for the diabetic on dialysis.[4,29] It is particularly gratifying that 74% of the diabetic patients that are alive following transplantation are active in work, school, or an avocation.

Evidence for recurrence of disease in the kidney transplanted to the diabetic should not be discouraging. Usually a period of 20 years elapses between onset of diabetes and clinical manifestations of diabetic nephropathy.

In conclusion, chronic hemodialysis is not a satisfactory alternative to transplantation for the uremic diabetic. Early transplantation offers the best chance for rehabilitation. Hopefully, the results can be improved as further experience is gained with transplantation in diabetics.

Acknowledgments

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HAVE YOU FULFILLED YOUR CME REQUIREMENTS?

The first triennium ends December 31, 1976.

Management of the Pregnant Diabetic

ROBERT F. CONIFF, M.D.* and EDWARD C. MAEDER, JR., M.D.†

Once actively discouraged, pregnancy in diabetes mellitus can now be successfully managed by a comprehensive team approach. Meticulous control of the diabetic state, prompt and aggressive attention to any medical and/or obstetrical complications, the use of newer methods of assessing welfare and maturity, combined with optimal timing and method of delivery result in substantial lessening of both fetal and maternal morbidity and mortality.

THE ASSOCIATION of diabetes and pregnancy imposes a well-established risk to the unborn and the newborn. This risk, as measured by a perinatal mortality rate, used to be between 10 and 15 percent. With good medical management, using a team approach, this mortality rate has been dramatically reduced in many major medical centers. The risk of pregnancy to the diabetic mother on the other hand, as noted by maternal mortality figures, is relatively insignificant with only a slight increase noted over the normal female population. As a result of improved management, the young female diabetic need no longer be discouraged from considering pregnancy, providing she is willing to accept the rigors of strict management throughout her pregnancy. The diabetic patient herself is the most essential member of the medical team and must be knowledgeable of her own care throughout the gestational period.

Some idea as to prognosis can be obtained through the Priscilla White classification of pregnancy and diabetes (Table 1). Obviously the prognosis is affected by the duration and severity of the disease, but the risk to the fetus increases as one proceeds down the classification. Classes A, B, and C offer the best fetal prognosis. Beyond Class C there is an increasing frequency of placental failure, intrauterine deaths, and congenital anomalies. Risks to the diabetic patient herself may be significant in cases of severe cardiopathy, nephropathy, and retinopathy. Pregnancy in these cases may actually be unadvisable and actively discouraged.

TABLE I

Classification of Pregnant Diabetics

Class A—Chemical diabetes—Abnormal glucose tolerance test
Class B—Onset after age 20, duration less than 10 years
Class C—C1—Onset age 10 to 19 years
    C2—Duration age 10 to 19 years
Class D—D1—Onset less than age 10 years
    D2—Duration more than 20 years
    D3—Calcification of vessels of the leg (macrovascular) disease
    D4—Benign retinopathy (microvascular disease)
    D5—Hypertension
Class E—Calcification of the pelvic vessels
Class F—Nephropathy
Class G—History of failed pregnancies
Class R—Malignant retinopathy
Class H—Cardiopathy

When conception occurs, the pregnant diabetic should search for good medical care, usually in a team setting, using facilities that most often can be provided in a regional perinatal center. The basic management plan most simply stated would encompass three principles: (1) Exact control of the diabetes throughout the gestation. (2) Avoidance of associated complications of pregnancy. (3) Proper timing and method of delivery of the fetus.

Endocrine and Metabolic Changes in Pregnancy

In a normal pregnancy, a number of endocrine and metabolic changes take place as a result of the presence of the placento-fetal unit. These changes include the following: (1) Increased degradation of maternal peptide hormones, especially insulin, by the placenta, (2) Biosynthesis of hormones by the placenta, including chorionic somatomammotropin (placental growth hormone or placental lactogen), estrogens, and progesterone, and (3) Increased removal of maternal fuels, especially glucose and amino acids, by the fetus, the latter being totally dependent on the maternal supply.

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See editorial, page 801.

Other well-documented, but probably less important endocrine changes include an increased level of maternal plasma cortisol and elaboration of a placental TSH-like substance by the placenta resulting in thyroid hypertrophy. The net results of these various changes are reflected in a state of relative insulin resistance in the mother demonstrated by the three to five fold increase in insulin secretion by the normal nondiabetic mother. In the pregnant diabetic, this is manifested by a progressive increase in insulin requirements as the pregnancy advances. The constant drain on maternal fuels created by the fetus also results in abrupt switches from the fed to the fasting state on the part of the mother.

Placental Growth Hormone

Placental growth hormone is a polypeptide hormone, chemically and immunologically similar to pituitary growth hormone, secreted by the syncytiotrophoblast. Like pituitary growth hormone, placental growth hormone seems to influence carbohydrate metabolism primarily by diminishing the effectiveness of maternal insulin. It also has significant lipolytic activity resulting in increased mobilization of free fatty acids from maternal fat deposits. Secreted primarily in the latter half of pregnancy and particularly in the third trimester, its concentration in maternal plasma increases ten fold or more during the last twenty weeks of gestation. Its net effect would seem to be that of reducing maternal glucose utilization and increasing the availability of glucose and amino acids to the fetus.

Estrogens and Progesterone

Increasing placental size is characterized by increasing placental secretion of both estrogen and progesterone into the maternal circulation. Although not completely understood, it has been reasonably well-documented that the administration of estrogens to normal individuals can result in a decline of glucose tolerance accompanied by an increase in plasma-insulin levels suggesting that estrogens also have an anti-insulin effect. The effects of progesterone on insulin secretion and action are not as well understood.

Cortisol

In addition to the increased secretion of estrogen, progesterone, and placental growth hormone characteristic of pregnancy, increased levels of plasma cortisol also typically occur. This increase in plasma level of cortisol is apparently due to both an increase in cortisol-binding protein (transcortin) and an increase in the plasma concentration of free (unbound) cortisol. The diabetogenic, anti-insulin effects of cortisol have been well delineated and may further contribute to the insulin resistance characteristic of both normal and diabetic pregnancy.

Second Half of Pregnancy

As a result of the endocrine function of the placenta described above, the second half of pregnancy is characterized by increased insulin resistance, diminished effectiveness of insulin, and a decline in maternal carbohydrate homeostasis. This situation is further complicated by the increasing degradation of maternal insulin by the enzyme insulinase in the progressively enlarging placenta. The net result is a marked increase in the demands for maternal insulin in both the normal and diabetic state during pregnancy.

Fuel Homeostasis

The fuel requirements for both energy and growth of the fetus are supplied completely from the maternal circulation. The rapid and continuous transfer of glucose across the placenta and its consumption by the fetus have profound effects on maternal carbohydrate and lipid metabolism. This continuous extraction of glucose by the fetus results in a tendency towards rapid shifts from the "fed" to the "fasting" state on the part of the mother. Clinically, this is demonstrated by a tendency in normal pregnancy towards maternal hypoglycemia after an overnight fast as well as increased ketogenesis in both normal and diabetic pregnancies. Thus, starvation ketosis and diabetic ketoacidosis are more prevalent in the pregnant state.

Pre-Pregnancy Counseling in Diabetes

Ideally, the diabetic woman will present herself for counseling before attempting conception. It is the duty of the family practitioner or internist, and the obstetrician, to be candid and firm with the patient while, at the same time, avoiding undue pessimism. Pre-pregnancy counseling should include an assessment of the nature and the duration of the diabetes, the patient's age, any existing complications (retinopathy, nephropathy), and any previous obstetrical history. The discussion should include the possible effects of pregnancy on the long-term complications of diabetes particularly retinopathy and nephropathy.

The need for a strict regimen of treatment throughout the pregnancy if a good result is to be expected must be stressed to the patient. There seems to be little doubt that the fetal outcome is determined primarily by the quality of diabetic control throughout the pregnancy. Other practical considerations include an honest appraisal of the extra time, expense, and effort involved on the part of the patient, including the likelihood of frequent visits to her physicians, more frequent and frequently expensive laboratory testing, the distinct possibility of additional and/or prolonged hospitalization, and, in all but gestational diabetics, the likelihood of delivery by cesarean section.

The patient should be instructed to maintain a careful menstrual history so that the time of conception can be accurately determined, this being of importance in determining fetal maturity and timing of delivery. Finally, the patient should be encouraged to undertake pregnancies at a younger, rather than an older age and to limit family size, hopefully to no more than two children.

Medical Management of the Pregnant Diabetic

Initial Evaluation of the Pregnant Diabetic

The initial visit of the pregnant diabetic should incorporate a complete history and physical examination. The physician must be especially alert for any evidence of existing chronic complications including retinopathy, nephropathy, hypertension, or cardiovascular complications. Attention should be paid to the patient's weight, usual diet, type and dosage of insulin, insulin injection techniques, and urine testing techniques. It is amazing how many newly pregnant diabetics present in the office with little or no knowledge of techniques for testing urinary levels of glucose and ketones. This is an ideal time, early in the pregnancy, to assess the patient's general understanding of her diabetic state and to recommend appropriate diabetic education classes if indicated.

The initial laboratory work should include a complete blood count and chemistry survey, with particular emphasis on blood glucose levels and renal function (serum creatinine, creatinine clearance). Fasting and two or three hour post-prandial blood sugars should be done to assess control. A routine urinalysis with emphasis on pyuria and albuminuria, accompanied by a urine culture to rule out asymptomatic urinary tract infection, are always done. At this time, the patient should also be referred to a nutritionist for appropriate instructions in her diet which will need to be adjusted to allow for fetal requirements. Finally, the importance of keeping the physician notified promptly of any and all problems that may arise must be stressed to the patient. Subsequent visits are usually at intervals of two weeks, increasing to weekly visits in the last trimester.

The Diabetic Diet in Pregnancy

The diet in pregnancy must take into account not only the metabolic requirements of the mother, but those also of the developing fetus. A total weight gain of about 24 pounds or approximately one pound per week during the last half of pregnancy is considered optimal for a good fetal outcome. Weight reduction diets are absolutely contraindicated during pregnancy since they can increase the risk of ketosis with its deleterious effects on the fetus.

A caloric intake of no less than 30 calories per kilogram of body weight is generally recommended. In most patients, this will come to 1800 to 2500 calories a day with a minimum of 2000 calories in most patients. Such a diet should include a minimum of 100 grams of protein, 40-45% of the total calories in carbohydrate, and the balance in fat.

The importance of regular meals and snacks must be emphasized. In particular, bedtime snacks are important because of the tendency towards over night hypoglycemia and ketosis. In gestational diabetes, diet alone frequently will maintain relatively normal glucose homeostasis. In many gestational diabetics over the age of 25 and in all insulin-dependent diabetics, insulin must also be used, but it is best to adjust the diet and insulin separately rather than simultaneously. Vitamin and mineral supplementation must also be taken into account in dietary prescriptions during pregnancy.

Insulin Therapy in Pregnancy

In gestational diabetes, diet alone will frequently suffice to maintain relatively normal fasting and post-prandial glucose levels. However, there is some evidence that fetal outcome can be maximized in gestational diabetics over the age of 25 years by the addition of insulin to the program. All insulin-dependent diabetics, of course, will require a continuation of insulin during their pregnancy. The use of oral hypoglycemics during pregnancy is contraindicated.

In most patients, NPH or Lente U-100 insulins are the basis of insulin therapy. An insulin regimen must, of course, be designed for each individual patient and may consist of a single morning dose of insulin with or without the addition of regular insulin, a split dosage program, a triple dosage program with intermediate acting insulins in morning and evening and regular before lunch, or, in some cases, a quadruple dosage program consisting of injections of regular insulin prior to meals and bedtime. Although some patients will remain under relatively optimal control on a single daily injection of insulin, there is an increasing tendency to employ split dosage programs in hopes of minimizing ketosis and the abrupt shifts of blood sugar levels so often characteristic of pregnancy.

In adjusting insulin, an attempt must be made to maintain euglycemia as much as possible, even at the expense of more frequent mild episodes of hypoglycemia. Such efforts to maintain euglycemia throughout pregnancy will be rewarded by normal sized infants and reduced fetal mortality and morbidity, a reward well worth the effort. Fasting blood sugars should be held as closely as possible to 100 mg% and two hour post-prandial blood sugars in the range of 120-140 mg% ideally.

Urine testing continues to be the most practical guide to insulin adjustments excepting those occasions where urine and blood glucose levels correlate poorly as a result of changes in renal threshold. The patient should be encouraged to adjust her own insulin, to supplement insulin as necessary, but at all times to keep in close contact with the physician when problems arise in diabetic control. If the patient is obviously under poor control when pregnancy is diagnosed, it may be advisable to consider hospitalization in order to achieve prompt and adequate control of the diabetes. As previously indicated, the physician and the patient should expect a progressive rise in insulin requirements during pregnancy with the exception of the first few months when a decreased appetite and nausea, with resultant decline in food intake, may actually bring about a decline in insulin requirements. Insulin requirements, however, will characteristically rise progressively from mid pregnancy reaching their highest level just prior to delivery. A decline in insulin requirements in late pregnancy may actually indicate fetal distress and may be an indication for immediate delivery.

In late pregnancy when lactose may appear in the urine, and in the presence of significant proteinuria, Clinitest tablet testing may give misleading results. Clinitest tablets measure primarily reducing substances and will give false positive reactions with lactose. Therefore, it is advisable to switch to a glucose-specific method of urine testing such as Diastix, in late pregnancy.

In cases where changes in renal threshold may be significant, a not uncommon finding in even normal pregnancy as a result of increased glomerular filtration rates, it may be necessary to specifically assess the correlation between blood and urinary glucose levels. This can be most easily accomplished by having the patient empty the bladder approximately one half hour before a blood sugar determination. After the bladder is emptied, the patient should drink one or two glasses of water and then empty the bladder again for testing at or about the time the blood sugar is obtained. This will allow for a fairly good assessment of the correlation between blood and urinary glucose levels. In those patients with markedly abnormal or altered renal thresholds, more frequent blood sugar determinations will be necessary since urinary levels of glucose will not be a reliable guide making insulin adjustments.

In brief, the goals of insulin therapy during pregnancy should be to maximize euglycemia in the mother at all times and to prevent the development of diabetic ketoacidosis. These goals will greatly enhance the possibility of a good fetal outcome.

Ketosis and Ketoacidosis in Pregnancy

Starvation ketosis and diabetic ketoacidosis are enhanced in pregnancy as a result of the switch from the "fed to fasting" state induced by the fetus as well as by the diabetogenic effects of the pregnancy itself. It is important to differentiate starvation ketosis from diabetic ketosis and diabetic ketoacidosis since their management will differ from each other. Starvation ketosis is most prone to occur during the early phases of pregnancy when anorexia and nausea may result in a decreased fuel intake. Clinically, it is characterized by normal or low blood sugars together with ketonuria. The obvious treatment is to supply needed fuel in the form usually of supplementary oral or intravenous glucose. This situation is not an indication for extra insulin.

On the other hand, diabetic ketosis and diabetic ketoacidosis result primarily from severe insulin deficiency and are characterized by greatly elevated blood sugars in combination with glycosuria and ketonuria. Diabetic ketosis and particularly ketoacidosis are a severe threat to fetal outcome, resulting in a fetal loss of 30 to 50%. Accordingly, this complication must be recognized and treated promptly. It is most apt to arise in a setting of poor control, infection, or in association with significant physical or emotional stress. Urinary tract infections in particular must be recognized and treated promptly during pregnancy. The treatment of ketosis and ketoacidosis in the pregnant diabetic is basically the same as in the non-pregnant diabetic, but immediacy of treatment and fetal salvage are of prime consideration. The importance of urine testing for ketone bodies cannot be over-emphasized to the pregnant diabetic.

Management at the Time of Delivery

The Class A or gestational diabetic is frequently allowed to deliver vaginally at full-term, i.e., 40 weeks, unless other complications develop. There is some indication, however, that gestational diabetics over the age of 25 should be delivered at an earlier time, much as insulin dependent diabetics. All insulin dependent diabetics should be hospitalized a minimum of 48 hours prior to their anticipated delivery, sooner if complications exist, in order that diabetic control be optimized. The patient is usually held NPO the night before anticipated delivery and a fasting blood sugar is obtained on the morning of delivery. An IV of 10% glucose and water is usually started in the early morning on the day of delivery to be run at a rate of approximately 100 cc/hour. If labor with vaginal delivery is allowed, continuous low dosage intravenous insulin with frequent blood sugar determinations is probably the best way of maintaining optimal control. If, as in most cases, cesarean section is planned, no more than 30% of the usual dose of NPH or Lente insulin is given on the morning of delivery and a stat blood sugar is obtained immediately following delivery in the recovery room. If at all possible, cesarean section should be scheduled for as early in the morning as is feasible.

Characteristically, insulin requirements drop rather drastically within hours after delivery and post-delivery hypoglycemia is quite common. Consequently, frequent blood sugar determinations and coverage with regular insulin is usually the best approach for the first 24 to 48 hours after delivery. NPH or Lente insulin therapy can be resumed thereafter and dosage adjusted upwards as indicated by the patient's diet and clinical progress. If the patient decides to breast-feed, an additional 300 to 400 calories and multivitamins should be added to the diet to allow for the lactation requirements of the newborn infant.

Obstetrical Management of the Pregnant Diabetic

The obstetrician when first evaluating a pregnant diabetic will immediately categorize the patient as a maximal risk. Initially some idea as to prognosis can be given by the patient's past diabetic history—recognizing the duration and severity of the disease. Likewise, the patient's past obstetrical history provides valuable information as to pregnancy risk. Initial calculation of the estimated date of confinement (EDC) is essential, as from this date a management plan is formulated and, indeed, the accuracy of the biochemical testing is dependent upon it. The normal clinical methods of estimating a due date also should be employed and, in addition, ultrasound beginning in the late second trimester may prove invaluable.

Avoidance of Complications of Pregnancy

In caring for the pregnant diabetic, one must be knowledgeable of the complications of pregnancy frequently noted in the diabetic. Table 2 denotes some of the most frequent complications. Some of these problems are preventable or at least readily detected and deserve special mention.

Recognizing that urinary tract infections are a frequent complication even in normal pregnancy, the diabetic should be screened periodically during her pregnancy with urine cultures.

TABLE 2
Complications of Diabetes and Pregnancy

1. **Infections—especially urinary tract**
2. **Toxemia (25%)**
3. **Hydramnios (20%)**
4. **Congenital abnormalities (6-10%)**
5. **Excessive size fetus**
6. ***Stillbirth***

Acute pyelonephritis poses special problems as to diabetic control, and can induce ketoacidosis.

The incidence of toxemia in the general pregnant population is 7%, while a greater than three times increase is noted in the diabetic. The finding of blood pressure elevation and proteinuria may take precedence over any previous management plan and may require immediate delivery of the fetus. One should likewise be aware of possible underlying diabetes in any patient presenting with severe toxemia.

In the delivery of a diabetic patient the physician has learned to frequently expect an infant of excessive size. Recognizing that traumatic delivery continues to be one factor creating a high perinatal mortality, heroics in attempting vaginal delivery should be avoided in cases where EFS is greater than 4,000 gms. Intrauterine growth retardation (IUGR) on the other hand can be encountered in diabetic pregnancies, especially those associated with maternal vascular complications. The prognosis for these infants is obviously poorer.

The sudden death of an infant in utero will always be the major dilemma the obstetrician faces. Recognizing that the risk of stillborn increases acutely in the last trimester, especially after 36 to 37 weeks, the physician must decide on the safest time to deliver the fetus. Often the patient will be hospitalized in the latter part of pregnancy where the fetus can be better monitored by frequent biochemical testing and biophysical monitoring. Past obstetrical history can never be overlooked and may indicate a need for earlier fetal monitoring. Clinical signs of decreasing insulin dosage, decreased fetal movement, etc. may alert the obstetrician to possible early intra-uterine demise.

Timing and Method of Delivery

As the diabetic patient approaches her EDC the physician must consider whether the fetus is at greater risk intra-uterine or extra-uterine. Clinical evaluation of the patient and fetus is not sufficient and thus monitoring of the fetus by biochemical studies and fetal monitoring is required. Serial estriol testing provides one study essential to detect impending fetal danger. This study is usually employed as the fetus approaches viability. The frequency of the testing is increased as the infant approaches maturity. Estriols have been shown to fall suddenly and dramatically in diabetics and therefore if used in cases of suspected fetal danger may need to be employed on a daily basis. The expense of this testing and the need for a skilled 24 hour laboratory are recognized drawbacks to this type of testing.

Antepartum fetal heart rate monitoring provides another method of evaluating the intrauterine status of the fetus. Stress testing or the oxytocin challenge test (OCT) often is employed over the same period where estriols are employed. A negative OCT, done on a weekly basis, has proved to be very valuable and may help delay the delivery of a premature infant.

When by clinical observations, by biochemical testing, or by antepartum monitoring, delivery seems advisable, it should be undertaken not withstanding the risk of prematurity. However,

TABLE 3

Management Plan—Pregnant Diabetic

I. Diabetic Education
    A. General diabetic education
    B. Pre-pregnancy counseling
    C. Contraception
II. Pregnancy and Diabetes
    A. Team approach
        1. Patient
        2. Internist
        3. Obstetrician
        4. Pediatrician
        5. Dietitian
        6. Physician assistant (nurse)
III. Obstetrical Management Plan (Diabetics B-F)
    A. Careful dating of pregnancy
    B. Close control of diabetes in clinic
    C. Avoidance of obstetrical complications
        1. Bimonthly visits until 30 weeks
        2. Weekly visits 30 weeks on
    D. Hospitalization
        1. Intercurrent problems
        2. 36-37 weeks (prior to delivery)
            a. Bedrest at home—34 weeks on
    E. Monitoring of fetus
        1. Weekly estriols 30-34 weeks
        2. Biweekly estriols 34-36 weeks
        3. Weekly stress testing (OCT) 32 weeks on
    F. Amniocentesis 36-37 weeks
        1. Delivery if L/S 2:1
    G. Delivery
        1. Vaginal
            a. Cervix ripe
            b. Fetal monitoring
        2. C-section
            a. Maternal and fetal indications
            b. Repeat C-section
            c. EFS greater than 4,000 gms.
    H. Postpartum care
        1. Six weeks postpartum exam (two weeks also post C-section)
        2. Contraception discussion
        3. Nursing visits (home) where indicated

in most cases the assessment of the fetus's status is not always clear-cut. In attempts to avoid prematurity, amniocentesis should be done to evaluate fetal maturity. The L/S ratio is most commonly measured and correlates well with pulmonary maturity. It has been shown that infants of diabetics may have delayed pulmonary maturation and thus avoidance of this problem is essential. Prior to any elective delivery of a diabetic pregnancy amniocentesis must thus be performed. In Table 3 a management plan for following diabetics in the last part of their pregnancy is included. Obviously, the feasibility of long-term hospitalization and daily fetal monitoring is difficult to assess. All patients should be hospitalized prior to delivery and whenever good diabetic control is needed. Assuming that the pregnancy is uncomplicated, delivery is planned for the 37th to 38th week assuming lung maturity is present via amniocentesis. Delivery may be vaginal or via cesarean section. In all vaginal deliveries the infant must be monitored and the diabetes carefully managed. Cesarean section would be indicated for the normal obstetrical indications, repeat cesarean sections and in cases where the EFS is greater than 4,000 gms.

Conclusion

The successful management of the combined challenge of pregnancy and diabetes requires an intensive team approach with a knowledgeable prospective mother playing the central role. Previously discouraged, pregnancy in diabetes can now be brought to a successful conclusion in most instances by a combination of meticulous control of the diabetes, prompt recognition and treatment of complications, careful fetal monitoring, proper timing and method of delivery, and close monitoring of the newborn infant of the diabetic mother. A suggested routine of management is presented in Table 3.

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Research in Human Diabetes—1976

FREDERICK C. GOETZ, M.D.*

Fresh evidence—especially genetic and immunologic studies—gives new life to an old idea: human diabetes is not a single entity, but a heterogeneous mixture of many disorders having in common one laboratory feature, an elevated plasma glucose level. Probably both mixed genetic and mixed environmental causes are present. Advances have been made in treating late complications, especially renal and retinal, but a truly preventive approach to these is badly needed. Continuing collaboration between the geneticist, the biochemist, and the clinician will be required.

THE BIG PROBLEM confronting someone attempting to summarize the current state of research in diabetes in 1976 is the enormous amount and variety of diabetes-related research going on in the world. Selection is inevitable, and I have chosen to present here some issues in diabetes research which seem important and fresh.

Obviously such selection is a very subjective matter. What I write here should be considered as heavily laced with personal editorial comments. Developments in Minnesota will be emphasized, as is appropriate for this journal. I will restrict my attention to spontaneous human diabetes.

Diabetes-related research will be considered under two broad headings: progress in understanding the nature of the metabolic disturbance of diabetes itself, and progress in the understanding and management of its complications.

Nature of Human Diabetes

One can regard diabetes (defined most simply as persisting hyperglycemia) as due to lack of adequate insulin secretion from pancreatic islets, or to a deficiency in the ability of tissues to respond to normal amounts of insulin.

(The possibility that excess of the second islet hormone, glucagon, may commonly play a role in the development of the diabetic state is an important one. For present purposes, it can be looked on as a special case of relative insulin lack.)

Prevention of diabetes is certainly the ultimate goal of all studies of the disorder. Understanding of the complex nature of diabetes is just beginning to dawn on us, as the result of new efforts to look at diabetes in large numbers of subjects.

Why Do the Islets Fail?

Primary failure of the insulin supply of the islets has been a dominant concept in the 1960's and 1970's. Some might say that it has been enough to explain almost all of the spectrum of human diabetes.[1]

The assumption that something going wrong with the islets is the first disturbance in many diabetic patients underlies the current excitement about the relationship between diabetes—particularly juvenile-onset diabetes— and certain human leukocyte antigens (HL-A). Knowledge of the HL-A system of antigens is a byproduct of human organ transplantation. It is clear that circulating leukocytes share with other organs and tissues a whole set of antigens inherited in a way precisely like that regulating the familiar ABO red blood cell groups. However, a number of different alleles have now been identified at each of four different genetic loci.[2] The best-known sets of antigens are at the A and B loci, but increasing knowledge is accumulating on two additional loci, currently designated C and D.

There is now clear evidence that some human disorders are considerably more likely to be recognized in persons carrying certain HL-A antigens in their tissues. An International Congress, attended by 800 investigators, has just concluded a four-day deliberation on HL-A and human diseases.

In respect to diabetes mellitus, it has now been reported from Denmark, England and the United States, including Minnesota,[3] that two antigens at the B locus—B8 and B W15—are associated with a significantly increased risk (perhaps three to five fold) for juvenile-onset diabetes. While this increase in risk with certain antigens is nowhere near as impressive as in some other conditions, notably ankylosing spondylitis, it provides one of the most solid fresh clues for the possibility that a genetic marker for diabetes can be identified which will allow—eventually—identification of persons predisposed to diabetes, before the condition is recognizable by any of the ordinary means.

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This is in an essential requirement for any truly preventive approach to what must be at least partly a genetic disorder.

There may well be, then, a "diabetic gene" operating in some families, and transmitted in fairly close linkage with some of the HL-A tissue antigens from one generation to the next. We must be clear about one point, however: the nature of that diabetic gene is totally unknown. At present it is attractive to assume that it might somehow express itself through an altered resistance to damage from an immunological disorder of some kind. This is in part because of the presence of immunological disturbances in the other HL-A-associated diseases. The mechanism might be something like this: exposure of the susceptible individual to the wrong kind of virus (mumps, Coxsackie B, or whatever), invasion of endocrine cells including the pancreatic islets by the virus, and persistence of the inflammatory reaction in the islet cells by sensitized lymphocytes which eventually destroy the islets through an autoimmune process.

The evidence that more than an occasional case of human diabetes is actually related to viral infection—or for that matter to infection of any sort—is fragmentary at present. Some of the most suggestive observations, keeping alive interest in this idea, are the incidence rates, month by month, of fresh cases of juvenile diabetes in Great Britain.[4] Through the excellent cooperation of physicians caring for the more than 50 million inhabitants, good reporting of new cases of juvenile diabetes has been provided for at least two recent years. There is a striking seasonal peak in both years, occurring late in the fall. Furthermore, most of the children accounting for these cases cluster in the age group 11 to 15 years. Age 11 means a change of school for most of the children in Great Britain. It is hard to think of a way of explaining these fascinating results, except through the action of an infectious agent. But we have no proof at all as to its nature.

Diabetes as Resistance to Insulin

While diabetes as islet failure has captured the imagination of most investigators in the last decade, the concept that at least some of human diabetes is due primarily to peripheral tissue failure to respond to insulin has never wholly died out. This possibility has long made sense as an interpretation of typical adult-onset diabetes, where measurable insulin levels in plasma are the rule.

Gerald Reaven and Jerrold Olefsky, at Stanford, have systematically worked to support this interpretation of diabetes. Using a standard drug infusion test, including a combination of glucose, insulin, epinephrine and a beta-adrenergic blocker (propranolol), they have observed the blood glucose response in 95 apparently typical, nonobese persons with adult-onset diabetes.[5] The response to insulin in these subjects varied markedly, from near-normal to very sluggish.

One can argue that they are observing variation in response, not to insulin, but to epinephrine or to the blocking drug. All the same, their work is important because it points to what may be basic differences in pathophysiology in what appear on the surface to be monotonously similar cases of ordinary diabetes.

Certainly adult-onset diabetes has to be accepted as of major importance, if only because of the millions of people who have it. This is underscored by the just-published study by Palumbo and others,[6] a pioneer report providing the first population-based incidence rates for diagnosed diabetes in a white United States community (Rochester, Minnesota). The overall incidence rate for a 25-year period was more than one case per 1000 people per year, and 95% of these were adult-onset (30 years or older at diagnosis)!

A flood of information from a new source is now demonstrating some of the underlying mechanisms through which resistance to insulin may develop. In the 1960's severe chronic resistance to insulin was generally associated with demonstrable high levels of circulating insulin-specific binding antibody in serum. Somehow such rather isolated cases seem to be rarer and rarer, in our experience in Minnesota and elsewhere. Instead, the study of insulin receptors on cell surfaces is providing new insight into the problem.

At the National Institutes of Health work especially from the laboratory of Jesse Roth and his associates is exploring the process by which insulin attaches itself to the surface of target cells before it expresses its hormonal action. Their method basically is an adaptation of the radioactive technique for measuring binding of insulin to antibody which was first developed by Berson and Yalow: specific binding of radioactive insulin to target cells (most commonly the circulating monocyte in the human leukocyte population) is demonstrated by its systematic displacement in the test tube by increasing amounts of unlabeled insulin. From the resulting displacement curves not only the number of receptors per cell but their binding characteristics to insulin can be deduced. A number of reports have shown that the familiar sluggish response to insulin in diabetes associated with obesity is accompanied by an apparent defect in insulin binding to cell receptors. In a fascinating recent report[7] it appears that in some special forms of chronic insulin resistance, probably of a genetic nature, insulin receptors are present but reduced in number, or that their affinity for insulin is reduced. Furthermore, in some cases circulating antibody to the receptors themselves (not to insulin) has been demonstrated.

Beyond the insulin receptor on the cell surface lies the enzymatic machinery of the cell and its nucleus. It is entirely likely that at least some forms of human diabetes have their origin in disturbances here, within the cell. At the moment, this remains an unexplored but potentially crucial area of knowledge.

Complications of Diabetes

The Diabetic Retinopathy Study and Minnesota

Just as difficult in their totally different way, are clinical studies aimed at precise evaluation of new methods of treatment. It is gratifying to emphasize the support given very recently by two independent studies to the use of photocoagulation in the treatment of advanced diabetic retinopathy.

The use of intense beams of light to treat retinal lesions—originally and most commonly white light produced by the xenon arc—began in Germany in the 1950's and by the late 1960's had been accepted by many ophthalmologists as clearly beneficial in diabetic retinopathy. Yet the variability of the course of this disorder is very well known. Spontaneous remission can occur. Furthermore, occasional evidence of obvious damage from photocoagulation has been observed. In such a situation, an organized and prospective clinical trial is mandatory if the questions of benefit and risk from a new treatment are ever to be settled.

In the British cooperative study, reported by Eva Kohner and her collaborators[8] there was as expected a marked variation in the course of untreated eyes as well as of treated eyes. However, after about three years of observation in over 300 subjects, the ultimate outcome for eyes treated for proliferative retinopathy clearly is better than for the untreated control eyes. In the subgroup primarily suffering from visual loss due to macular edema (a lesion which has only recently become familiar as a major cause of blindness) the benefits of photocoagulation were especially clear.

The American counterpart, the Diabetic Retinopathy Study (DRS), now confirms and extends the favorable judgments of the British study.[9] John Harris of the University of Minnesota was one of the chief planners of the DRS. Using the argon green laser as well as the xenon white arc light, and employing a vigorous ablative approach to the peripheral retina (with an unavoidable loss of some peripheral vision), two years of observation in more than *1500 subjects* showed that progression from useful vision to blindness can be sharply reduced by photocoagulation.

In the untreated eyes one eye in six has progressed to blindness under observation; in the treated eyes only one eye in sixteen has lost useful vision.

But the DRS is proving to be of importance beyond simply establishing the benefit of photocoagulation as applied in certain specific ways. Analysis of the extensive data from the study points to the special importance of the location in the retina of proliferating new vessels. It seems clear that new vessels sprouting from the disc may be especially likely to bleed and lead to advanced complications and blindness. New vessels elsewhere in the retina, although potentially serious, appear to have not quite the bad prognosis of the disc vessels. Clearly, the general physician caring for the diabetic patient will need to sharpen his observations of the retina in the patients he is caring for daily.

The DRS affords a very clear example of how planned research—and a carefully planned clinical trial in particular—can yield extremely valuable information both on the natural history of an important disorder and on the best way to treat it. Physicians in Minnesota can take satisfaction in the part they have played in supporting the study at the University of Minnesota, where one of the most active units of this nation-wide cooperative study is based.

Diabetic Kidney Disease

This is the other dramatic and distressing problem peculiar to long-standing diabetes. Minnesota clearly is a leader—probably a world leader—in the application of modern kidney transplant techniques to the diabetic patient. Together, Mayo Clinic and University of Minnesota account for about half of such transplants which have been performed since mid-1969.[10,11] My personal impression is that many other transplantation groups continue to watch the Minnesota experience and have hesitated to embark on this program themselves. The University of Minnesota and Mayo Clinic experiences are in agreement in all important aspects: the overall survival is somewhat less good than in the nondiabetic transplant patient, but the five-year survival appears to be approaching a satisfying value of 60%. About two-thirds of such patients return to an approximately normal life and many have returned to work. The quirks of our current economic and especially health insurance plans have kept some from working who might otherwise be fully employed. Even though very suggestive evidence of return of diabetic vascular disease has begun to appear in biopsies from the transplanted kidneys,[12] they continue to function well for as long as seven years post-transplant.

Thus, the general value of the procedure seems clear. However, it certainly must be looked at as a desperate end-stage approach, costly and troublesome, to the problem of diabetic nephropathy. In this respect it could be compared to the iron lung as a treatment for poliomyelitis. Clearly, what would be far more desirable in the long run would be a simple preventive approach to diabetic kidney disease. There is not the least clue to this on the horizon at present—other than the vexed question addressed below.

Clinical Management of Diabetes and the Prevention of Vascular Complications

After many years of doubt, frustration and controversy, a general feeling (I would hesitate to call it a ground swell) seems to be apparent in the last year or so that the balance of scientific evidence has gradually tipped in favor of the view that metabolic control of human diabetes can indeed prevent vascular complications. A typical symptom of this feeling is the recent editorial written on behalf of the American Diabetes Association, expressing the feeling of many physicians that the burden of proof now is on those who maintain that there is no connection at all between diabetic regulation and occurrence of vascular disease.[13]

It seems to me that the position taken in this editorial is probably exactly right but just a little premature—a little bit ahead of the evidence. Although animal studies are supportive, the only really appropriate clinical study that can be cited is an intriguing one recently published from Paris.[14] In this carefully designed study, early diabetic retinopathy was less apparent after two years of treatment with four injections of insulin a day, than it was in a randomized control group treated with one injection of insulin a day. So far, so good. The problems and the limitations of the study are unfortunately considerable. The number of patients in each treatment group (twenty-one) is terribly small in comparison with the large numbers described above in the photocoagulation studies—where much evidence indicates that the variability of retinopathy is so great that many hundreds of patients are needed for solid conclusions about the effects of treatment. Also, in the French study the retinopathy was relatively early and of uncertain relationship to the vision of the patients. Finally, although significant differences in glucose levels in urine and plasma were documented, the interval of observation of the patients (once every three months) leaves large room for uncertainties about day-today control. In any case even the patients on four injections of insulin per day did not achieve normal glycemia.

The Paris study nevertheless is an excellent pioneering effort which should be amplified and extended. The trouble is that such a study is enormously difficult and costly and not least of all requires enormous patience on the part of the investigators.

The University Group Diabetes Study still stands as a sobering example to anyone planning such a study. Here in a study of adult-onset diabetes, with 200 patients in each of five treatment groups, it has proved impossible over nearly 15 years of followup to show distinct benefit from conventional methods of treatment appropriate to this type of diabetes.[15]

Such results do not mean that appropriate metabolic treatment could not alter the course of vascular disease. They simply mean that it has been difficult to demonstrate this with methods now at hand. It is cogent to keep in mind the great difficulty of demonstrating benefits in coronary heart disease from lowering serum cholesterol.[16]

As physicians, we have plenty of grounds for advocating a philosophy of close control of diabetes to our patients. As scientists, we need to hold on to our humility, realizing that detailed proof of clinical hypotheses is often very difficult to provide, and that tomorrow's knowledge may make today's rational practices completely beside the point.

Conclusions

Among the important aspects of human diabetes which I have *not* discussed I can mention these:

1. The new and challenging field of research in the delivery of health care, in which diabetes can provide a nearly ideal test case;
2. The vastly improved understanding of blood (and urine) glucose levels in treated diabetic patients which have come from the 48-hour continuous glucose monitoring studies of John Service and George Molnar at Mayo Clinic.[17]
3. The latest trials in human islet transplantation;[18]
4. Diabetic neuropathy, and the intriguing evidence (though mostly in animals) that sorbitol and other glucose derivatives may contribute to its development.

What I have wanted to bring out especially are these ideas:

1. Human diabetes of the common variety gives signs of breaking up into a cluster of disorders superficially indistinguishable but with differing underlying mechanisms and inheritance patterns.[19] The analogy to hyperuricemia is an appealing one.[20]
2. Our approach to the advanced complications of diabetes is one of desperation, reminiscent of the iron lung and poliomyelitis. Simple preventive treatments for retinopathy, nephropathy and neuropathy are much needed. Careful clinical trials are a painful necessity in evaluating results of treatment in these complex and variable disorders.

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Diabetes Mellitus

A Plan for the Physician and His Patient

G. E. COTTON, M.D.*

A plan for management of diabetes mellitus is presented to physicians and patients. A method for correcting physiologic abnormalities as completely as possible using currently available modalities of treatment is described. Patient education is an essential element of treatment.

THE TERM DIABETES MELLITUS is used clinically to describe different entities. These entities have in common an elevated blood glucose. Diabetes and[1-3] its effects on those afflicted with it,[4-5] both in the form of acute management problems and chronic complications, are well known. Also known is a considerable amount about the pathophysiology of diabetes and etiologic relationship of metabolic abnormalities to development of its chronic complications.[6-12] Using this knowledge and currently available methods of therapy, one can plan a logical and effective program for treatment of the patient with diabetes mellitus.

Two concepts are especially important. First, the patient's and the physician's knowledge of diabetes mellitus must be similar, differing only in quantity and detail rather than quality and concept. Second, while it is the physician's responsibility to see that the patient is properly educated, the patient must assume full responsibility for day-to-day treatment of his diabetes.

Basis for the Plan

Insulin deficiency remains the central consideration in diabetes mellitus,[13,14] and although other factors are undoubtedly important, an understanding of key aspects of normal insulin physiology plus the role of insulin deficiency in the genesis of the chronic complications of diabetes mellitus forms the basis for planning an optimal program of treatment.

Insulin Physiology

Plasma insulin levels normally increase and the blood glucose and free-fatty acids decrease slightly at the sight and smell of a meal.[15-17] Upon ingestion of food, an enteric hormonal signal stimulates insulin release so that plasma insulin levels increase before there is a measurable rise in blood glucose.[18] This early phase of insulin secretion mediated through neural action and the entero-beta cell axis is especially important, as it insures that approximately two-thirds of the absorbed glucose is taken up by the liver on the first passage of blood through the organ, and sets the stage for the magnitude of the delayed phase of insulin secretion. These mechanisms, which assure that "insulin is there and waiting" prior to the arrival of glucose from the gastrointestinal tract, prevent excessive post-meal hyperglycemia. The delayed or final stage of insulin secretion is due to direct beta cell stimulation by the rising blood glucose.[19]

In diabetes absolute deficiency of insulin, delay in the time of insulin release or peripheral blockade of insulin action—alone or in combination—results in hyperglycemia. Classified thus, according to the major physiologic abnormality, the terms insulinopenic, insulinotardic and insulinoplethoric are conceptually useful and correspond closely with juvenile onset and adult onset diabetes mellitus, and the obese hyperglycemic patient respectively.

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Deficiency of insulin *action* results in several abnormalities in glucose metabolism, including formation of polyols,[6-8] excess production of glycoproteins which are both qualitatively and quantitatively abnormal,[9-11] and abnormalities in glycosaminoglycan production.[12] Slow accumulation of these substances over a period of years may correlate with the eventual manifestations we recognize clinically as evidence of the chronic complications of diabetes mellitus.

The Plan

The treatment program is designed to correct known deviations from normal physiology as completely as possible. As the pathophysiology of each type of diabetes differs, the treatment program is designed accordingly, always with the similar goal of correcting insulin deficiency. Consideration of the three familiar variables influencing the level of blood glucose; namely, food, exercise, and insulin; plus education of the diabetic patient to enable him to adjust each of these variables as needed, form the essentials of treatment.

Insulinopenic Diabetes

Dietary therapy for this group is important but follows rather simple guidelines. The total caloric intake should be sufficient to maintain body weight at an ideal level. No special qualitative alterations are made unless there is an associated problem such as hyperlipoproteinemia which does not respond to control of the patient's diabetes. Meals are divided into six feedings daily —three meals plus mid-morning, mid-afternoon, and bedtime snacks. All of these feedings are relatively small and concentrated free sugars are avoided in order to minimize blood glucose elevations. Special emphasis should be placed on supplying a diet which will provide for the diabetic the same nutritional values recommended for non-diabetics of similar age, height and weight and should be compatible with the family's food habits and financial resources.[22]

A regular daily exercise program is recommended and should consist of an amount of exercise that is comfortably tolerated by the patient. In early childhood, close regulation of exercise is not possible and should not be attempted. Alteration of food intake and to some extent insulin dosage will be needed to compensate for variations in activity in this age group.

Insulin replacement is essential in this type of diabetes and the subcutaneous route of injection is the only practical one for chronic administration; thus, delivery of insulin is crude when compared to normal physiology, as the increase in insulin levels in response to normal stimuli is totally lacking and solely dependent on the rate of absorption from a depot site. Nevertheless, every effort is made to design a program that will provide insulin action as physiologically as possible, i.e. insulin "there and waiting" for glucose arrival and to correspond to time of glucose presence. The value of this method of insulin administration is indicated in several excellent studies.[22-25]

A major consideration in therapeutic use of insulin is the time following injection during which it exerts its effect. These time action curves of insulin vary somewhat from patient to patient, with prolongation of the time of peak insulin activity as the total dose injected increases. In the absence of renal insufficiency, the data provided by the study of Dr. Ginsberg, et al., is clinically useful (See Figures 1-5).

The basic plan of insulin therapy includes neutral Regular and NPH insulins—both in U100 concentration. These insulins are very compatible when mixed together, each retaining its individual time action properties. It is obvious from the above data that neither of these insulins given in

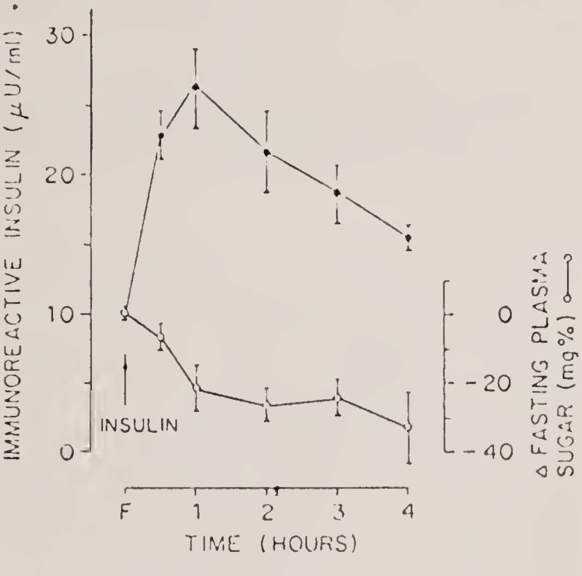

Fig. 1. Serum insulin and plasma sugar (change from fasting level) in healthy subjects following subcutaneous injection of 10 U regular insulin. The values are mean ± SEM. Reproduced from J CE & M with permission of Dr. S. Ginsberg and J B Lippincott Co. Vol. 36, #6, 1973.

a single daily injection, either alone or in combination, can prevent insulin deficiency throughout the 24-hour period. In order to keep insulin deficiency at a minimum, it is necessary to take more than one injection daily. While an injection of regular insulin before each meal is satisfactory, the inconvenience of three or four injections per day may be undesirable. Our plan for routine use is two injections per day, the first one-half hour before breakfast and the other one-half hour before supper, using Regular and NPH insulin mixed together in the same syringe. If the patient in question is a new diabetic, multiple injections of Regular insulin alone are given through the day until an estimate of total daily requirement can be made. If the patient is a long-standing diabetic and the program is to be changed, an amount slightly less than the dose previously given in a single injection should be used. Initially, two-thirds of the total dose is given in the morning and one-third in the afternoon using 50% Regular and 50% NPH insulin. This basic program is then slowly changed to meet the requirements of the individual diabetic. The diabetic *must* be taught how to adjust his own dose of insulin so that optimal control can be obtained

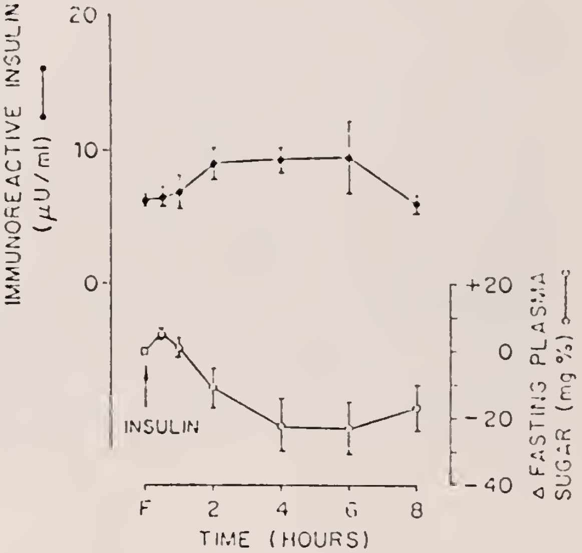

Fig. 2 Serum insulin and plasma sugar (change from fasting level) in healthy subjects following subcutaneous injection of 10 U NPH insulin. The values are mean ± SEM. Reproduced from J CE & M with permission of Dr. S. Ginsberg and J B Lippincott Co. Vol. 36. ±6, 1973.

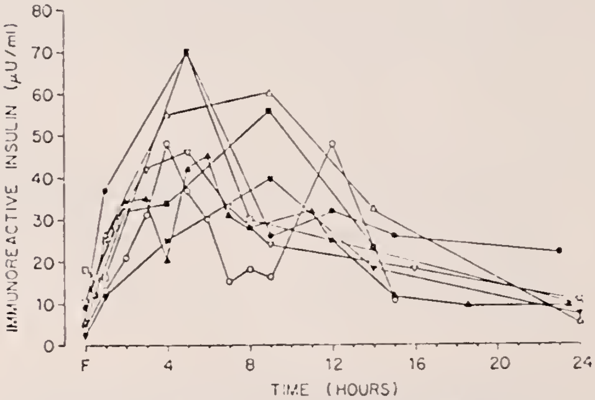

Fig. 3. Serum insulin concentration during a 24-hr period in diabetic patients following subcutaneous injection of NPH insulin (15-50 U). Reproduced from J CE & M with permission of Dr. S. Ginsberg and J B Lippincott Co. Vol. 36, ±6, 1973.

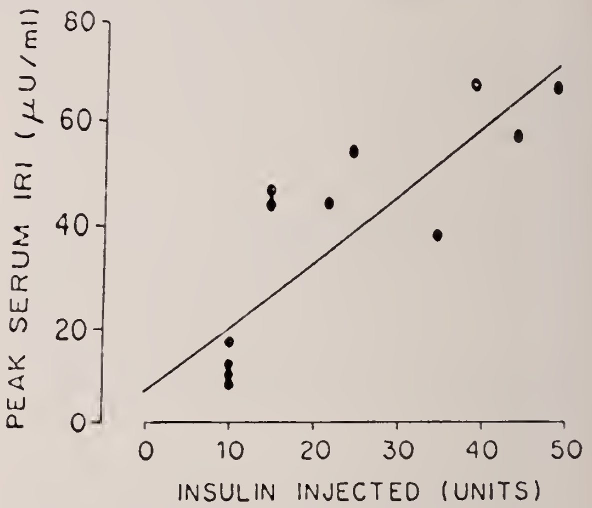

Fig. 4. Correlation of insulin dose and peak serum insulin concentrations in healthy subjects and diabetic patients following subcutaneous administration of NPH insulin (10-50 U). The regression equation was y = 1.3 × +8, p <0.02. Reproduced from J CE & M with permission of Dr. S. Ginsberg and J B Lippincott Co. Vol. 36. ±6, 1973.

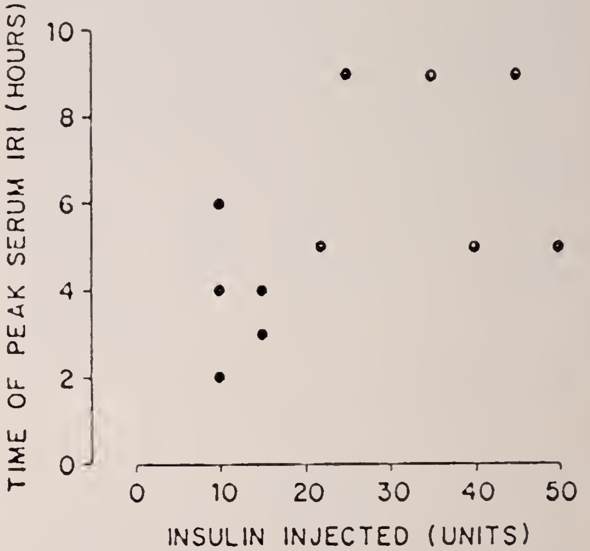

Fig. 5. Relationship of injected dose of NPH insulin and time of occurrence of peak serum insulin concentrations in healthy subjects and diabetic patients. The insulin (10-50 U) was injected subcutaneously. Reproduced from J CE & M with permission of Dr. S. Ginsberg and J B Lippincott Co. Vol. 36, ±6. 1973.

in his particular environment, according to his lifestyle and to compensate for fluctuations that may occur from time to time.

The rules for adjusting insulin dosage are simple and basically two. First, changes are small—*one or two units of one insulin only;* and second, they are infrequent—no more often than every 2nd or 3rd day. These changes may be made as many times as necessary until optimal control is reached. The initial basis for changing the insulin dose is the record of urine tests. All tests are done on second voided urine specimens and reagent strips or clinitest tablets are satisfactory. (First voided urine tests may be recorded if they are negative—if positive for glucose, a second specimen should be tested in a few minutes and the second value recorded.) The ideal urine record is one that is entirely negative for glucose in a patient who is not experiencing hypoglycemic reactions. This may not be possible and thus the goal changes to that of obtaining the largest number of negative tests possible without having hypoglycemic reactions. Once the urine record is at its best, periodic blood glucose determinations (often with Dextrostix at home) are recommended for finer adjustment of the insulin dose.

The urine test is kept in the following form:

Date	* Morning	Noon	* Afternoon	Bedtime	Comments
	Change P.M. NPH to adjust this column	Change A.M. Regular to adjust this column	Change A.M. NPH to adjust this column	Change P.M. Regular to adjust this column	

*Insulin injections given 20-30 minutes before breakfast and supper.

Changes in insulin dosage are made according to *patterns* of positive tests noted in the urine record. If the urine tests in any vertical column are persistently positive, even 1 or 2+, the insulin that affects that column should be increased one or two units. If the pattern persists, the insulin dose is increased again in two or three days. Changes are made as many times as necessary until the urine becomes glucose free or until hypoglycemic reactions occur. The specific insulin to be changed for each pattern is indicated in the appropriate column of the urine record; i.e. if the morning urine tests are persistently high, the NPH taken before supper is increased.

Hypoglycemic reactions are to be avoided if possible. Following a hypoglycemic reaction, a period of insulin resistance lasting a few hours to a day or more is present[26] (Somogyi effect). Thus, it is usual for the first few urine tests after a hypoglycemic reaction to be positive for glucose and the blood glucose is regularly elevated the following day. This does *not* indicate the need for more insulin. On the contrary, hypoglycemic reactions indicate the need for reduction of the insulin dose. The insulin which is having maximum activity at the time the hypoglycemic reaction occurred is determined by consideration of its time-active curve and a reduction of one or two units every one to two days is made until no further reactions are experienced. After a two or three day period during which there have been no hypoglycemic reactions, the insulin dose can again be adjusted slowly upwards as indicated by the urine record.

The use of insulin during illness requires special comment. Illness virtually always increases the requirement for insulin even if the patient cannot eat and food is not ingested; therefore, insulin should *never* be omitted during illness. If the urine is free of glucose and food cannot be eaten (nausea, etc.) then one-half the usual dose should be taken. If the urine contains glucose in small amounts (1 to 2+), the usual dose should be taken. If larger amounts of glucose are present, especially if ketonuria is present, the dose of regular insulin is increased. The amount of increase should be advised individually by the patient's physician. During illness, additional injections of regular insulin should be given at noon and at bedtime if the urine glucose remains 3 or 4+, especially if ketonuria persists. This may necessitate four or more injections per day, but is necessary to prevent diabetic ketoacidosis and coma. Once recovery occurs, the insulin dose should be reduced to pre-illness levels in order to prevent hypoglycemic reactions.

Education of the diabetic patient in management of his disease is best provided on an outpatient basis at a diabetes education center. Instruction in all aspects of management of diabetes can be provided over a five-day period at available centers in Minnesota.* The patient who has known diabetes should attend the education program as soon as possible. The new patient benefits most if he has been treated intensively in a hospital and instructed in the basic management techniques and then allowed to go home for two or three months prior to attending the diabetes education center. During this interim period, he becomes emotionally adjusted to the problems of being diabetic and becomes aware of difficulties in its management. The comprehension and retention of the material presented at the education center is much greater than it is when intense instruction is attempted immediately following diagnosis.

Insulinotardic and Insulinoplethoric Diabetes

The insulinotardic and insulinoplethoric diabetics can be considered together. As all of the insulinoplethoric and 90% of the insulinotardic patients are obese with resultant peripheral blockade of insulin action,[27] the primary form of treatment is dietary. Weight reduction results in reversal of the insulin receptor blockade with return of insulin sensitivity. Indeed in the absence of weight reduction, all additional forms of therapy are relatively ineffective and adequate control is often not obtainable.

Patients in whom hyperglycemia is corrected by diet require no additional therapy. In those insulinotardic diabetics in whom hyperglycemia (FBS above 115 mg/dl or two hour p.c. blood sugar above 130 mg/dl) persists despite adequate dietary therapy, the second line of treatment; namely, drug therapy should be introduced. The sulfonylureas are useful and effective in this circumstance. If the use of these agents results in normal fasting blood glucose levels and in two hour post-prandial blood sugar levels of 130 mg.% or below, the oral agent is continued. This agent is given in an effort to correct the timing of release of insulin towards normal, initially increase the absolute amount of insulin secreted[28-29] and to decrease the peripheral blockade of insulin action at the level of the insulin receptors.[30]

If the above conditions are not attained, insulin therapy is begun and in general follows the same concepts as outlined above for treatment of the insulinopenic patient.

In the experience of all diabetologists, there is a significant number of patients in whom attempts to attain adequate weight reduction is unsuccessful. In this group, all additional methods of controlling hyperglycemia may also be relatively ineffective. Oral hypoglycemic agents may lower the blood glucose suboptimally and the value of their use in this circumstance is unknown. Insulin therapy is also relatively ineffective in the obese, as its effects are blocked peripherally, and the lipogenic properties of insulin may only aggravate the problem. It must be emphasized that in the obese hyperglycemic patient, if weight reduction is not attained fully, effective alternative therapy may not be available.

Presented above is a plan for the treatment of the patient with diabetes mellitus. This approach will provide as precise control of the diabetic state as is currently available using conventional methods of therapy. The single most gratifying facet of the plan is the patient's reaction to the educational experience. Patients regularly express considerable relief of their fears of the unknown in regard to diabetes, and satisfaction and confidence in the ability to manage their problem in the future. An evaluation of the patient's knowledge by retesting six months to four or more years after completion of their educational experience has revealed test scores as high or higher than those at the time of completion of the course in most cases.[31] This indicates continued interest and motivation on the part of the patient plus an ability to interpret the diabetic literature, which they are continuing to read.

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*Diabetes Education Centers—contact ADAM, 7601 Bush Lake Rd., Minneapolis, Minnesota 55435.

References will be found on page 765.

Education of the Diabetic Patient

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An essential component in the treatment of diabetic patients is to teach them how to manage their disease on a daily basis. Guidelines that the physician and his health care team can use to educate the diabetic patient are described.

WHAT IS ACETONE? Why can't I take a pill of insulin rather than a shot? How can I avoid insulin reactions? How can I follow my diet while eating in a restaurant? These are some of the questions that diabetics ask frequently.

Each physician has some diabetic patients who don't comply with their management regime. Many patients do not comply because they don't understand how to manage diabetes. They have many questions as evidenced above or they may not be aware of all the factors entailed in safe care of diabetes.

How to Teach Patients?

To alleviate these problems, education of the diabetic should be integrated continuously into every facet of his/her health care from the time of diagnosis. For the maximum effect of learning about diabetes, the education should be planned, organized, and systematically based on the patient's needs. To accomplish this, the educator should begin by interviewing the patient to determine his knowledge, techniques, emotional adjustment, educational level and lifestyle. Based on this information, the educator would then assess the patient's learning needs and establish a teaching plan. In implementing the teaching plan and doing the teaching, a variety of teaching-learning approaches can be used; one-to-one teaching, group classes, group support sessions or self-paced programmed instruction. Integrating audio-visual aids, practice sessions, and discussion throughout the teaching process enhances learning. While teaching the patient, evaluate his response to the information at all times. Did he understand what was taught? Can he apply the information to his management and lifestyle? Dependent upon the evaluation, the teaching strategy may need to be altered to further meet the patient's needs.

What to Teach the Patient

The following objectives describe the optimum amount of information a diabetic patient should know about his disease. The educator can modify these guidelines for each patient based on his age, type of diabetes, treatment plan, learning needs, educational level, and emotional adjustment.

Diabetes Education Center
Health Education for Living Program, Inc.
4959 Excelsior Boulevard
Minneapolis, Minnesota 55416

Objectives for Diabetic Patients or Parents

1. To Demonstrate a Basic Understanding of Diabetes Mellitus:
    - ___ Understands functions of the beta cell in pancreas.
    - ___ Understands action of insulin in the body.
    - ___ Can differentiate between juvenile onset and insulin-dependent and non-insulin dependent adult onset diabetes.
    - ___ Knows the significance and symptoms of hyperglycemia.
    - ___ Knows how to balance insulin, diet, and exercise.
    - ___ Knows normal blood test values.
2. To Demonstrate Accuracy in Testing Urine for Sugar and Ketones:
    - ___ Knows significance of urine testing.
    - ___ Is able to give a simple explanation of renal threshold.
    - ___ Uses second voided specimens.
    - ___ Is able to accurately perform urine tests.
    - ___ Performs tests at proper times.

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— Is able to accurately interpret urine test results.
— Knows where to store urine testing materials to maintain potency.
— Maintains accurate urine testing records and knows significance of record-keeping.

3. To Understand the Medications Used for Controlling Your Diabetes:

Oral

— Knows type of medication.
— Understands action of medication.
— Knows time action of medication.
— Knows when to take medications.
— Knows proper dosage.

Insulin

— Knows type and concentration of insulin.
— Knows onset, peak and duration of insulin.
— Knows difference between U-40, U-80, and U-100 insulins.
— Knows how to store insulin when at home or traveling.

4. To Demonstrate Accurate Administration of Medications:

— Knows type of syringe needed for injection.
— If using glass, knows how to sterilize and store syringe.
— Can adequately draw up both a single and mixed dose of insulin.
— Can adequately perform injection of insulin.
— Properly disposes of syringe and needle.
— Is able to use all injection sites.

5. To Have a Basic Understanding of Hypoglycemia (Low Blood Sugar):

— Understands basic physiology of hypoglycemia.
— Knows probable times that reactions occur.
— Knows causes.
— Knows symptoms.
— Can adequately treat reactions.
— Knows how to prevent reactions.

6. To Have a Basic Understanding of Hyperglycemia (High Blood Sugar):

— Understands basic physiology.
— Understands causes.
— Understands symptoms.
— Knows how to adequately treat hyperglycemia.
— Knows how to prevent acidosis.

7. To Have a Basic Understanding of Long-Term Complications:
Has basic knowledge of:

— Retinopathy
— Neuropathy
— Nephropathy
— Atherosclerosis
— Knows importance of control in decreasing or preventing complications.

8. To Understand the Diabetic Diet:

— Explains the relationship of diet in the total management program.
— Knows the foods and portion sizes in the food exchange groups.
— Knows his own meal plan.
— Able to plan menus based on individual meal plan.
— Applies food labeling information to the diet.
— Modifies the diet for days of illness.
— Understands the relationship of alcohol in the diet.
— Can adapt the diet for:
    — Eating Out in Restaurants
    — Traveling
    — Exercise
    — Special Occasions
    — Nutritional Labeling

9. To Understand the Necessity of Wearing Diabetes Identification:

— Uses diabetic identification card and bracelet or necklace.
— Knows importance of informing significant others of his diabetes.

10. To Be Aware of Resources Available to the Diabetic:

— Knows availability of Diabetes Associations.
— Knows availability of diabetes camps.
— Knows availability of public health nurse.
— Knows availability of diabetes education resources.

11. To Understand Practices of Personal Hygiene

— Understands importance of daily skin care.
— Knows medications and procedures to avoid.
— Knows how to choose foot wear.
— Understands importance of mouth care.

12. To Understand the Importance of Followup Care With the Following:

— M.D.
— Dentist
— Ophthalmologist
— Dietitian

When to Teach the Patient

Education of the patient with diabetes mellitus and his family is a staged process. Too much information too soon can cause needless anxiety in the patient and family and wasted time and frustration for the educator.

During the diagnosis and/or hospitalization stage of diabetes, the absolute minimum of information must be imparted. A brief description of diabetes and the fact that it cannot be cured but can be controlled is about the maximum amount of information that can be assimilated during this anxiety-laden time. Brief, simplified pamphlets supplied by the various diabetes associations and pharmaceutical companies may be given to the family and patient to peruse at their own rate.

Anxiety is probably the single most difficult obstacle in educating the diabetic. Because of the anxiety, information must be simple, repeated verbally, visually demonstrated and return demonstrated by the patient.

In the Minneapolis-St. Paul area, the Twin Cities Diabetes Association offers a hospital visitation program to help lessen the anxiety of the newly diagnosed diabetic and his family. By calling the association, specially selected persons with diabetes or their family members will go into the hospital to talk with patients and/or families. A diabetes nurse educator is present at all visits to answer any medical questions that may arise. This has proven to be a tremendous support to patients and families.

After the patient's diabetes has been stabilized, *gradual* extension of information is needed. Innumerable educational opportunities present themselves in a hospital setting. To effectively utilize this setting, an educational care plan carries as much importance as the medical care plan. The teaching plan should be drawn up by the team that will be doing the educating. This usually consists of the physician, nurse and dietitian. Many hospitals also include a pharmacist, a social worker and any other health professional who might enhance the educational experience.

The educational care plan should include both task and conceptual goals and objectives. A check list is of great value in communicating the level of education to the team and other staff members.

In the daily visits with the physician, *brief* simplified explanations of the nature of the diabetes, acidosis, and hypoglycemia should be given. Concurrent literature should be left with the patient and family to reinforce and supplement the verbal information. The nurse and dietitian will be available to answer questions as they surface and elaborate on the information given by the physician.

The morning medication is an excellent opportunity to discuss timing and action of medications.[1] For the initial injection of insulin, brief explanations of insulin preparation and injection are needed. Leave a syringe and practice bottle of insulin with the patient to examine. In addition to the verbal instruction, leave written instructions on insulin preparation and injection with the patient and/or family so they may practice at their leisure and become familiar with the equipment. Have family members and patients prepare the injection under supervision. Having the patient inject someone with sterile sodium chloride is a real confidence-booster. The patient should be in charge of preparing and giving the insulin as soon as possible after diagnosis (age permitting). At least one other family member should be adept at insulin administration.

Meal and snack times offer excellent opportunities to reinforce the dietitian's meal planning instructions. This is a prime time to reinforce the previous information given on insulin action and peak times. If the information is communicated in logical time sequences and incorporated into the daily activities, it tends to take on a greater significance.

Urine testing is again an opportunity to demonstrate and have the patient return the demonstration. This will, as discussed in insulin administration, allow correction of any errors in procedure and will increase the patient and family member's confidence in their ability to effectively perform these tasks. To increase the probability that patients will test their urine on a routine basis, explain how the tests will be utilized. When changes in insulin doses are made, showing a relationship between the high urine sugars and the subsequent dosage changes, reinforces the importance of testing. It is important to teach the patient that with time, he and his family will be able to look at the urine tests, see patterns developing and make minor changes in the dose. This not only communicates the responsibility for self-care to the patient but also the confidence the medical team has in the patient's ability to manage the diabetes. This lends credence to the instructions that urine testing in record books (available from diabetes associations and the pharmacy) is of value and should be utilized.

If at all possible, the patient on insulin should be allowed to experience an insulin reaction while in the controlled setting of the hospital. This will decrease the fear factor that just an explanation of reactions could portend and serves as the basis for a teaching opportunity.

Working in some type of exercise program with the hospital setting will also decrease anxiety for the patient when he is out of the hospital. Many hospitals work out daily exercise programs with the physical therapy departments. This serves as an active teaching moment that will decrease the patient's anxiety levels.

Although dietary management is essential for all diabetics, patients have found adherence to their prescribed diet the most difficult aspect of control.[2] Food is an integral part of our society and diabetics object to being different from their peers because they cannot eat the foods which are part of their cultural, social, and economic background. A thorough understanding of their diet and rationale of dietary treatment will improve the patient's adherence.

The dietitian's initial visit with the hospitalized diabetic should include a brief explanation of her role and an introduction to his diet. As with the nursing aspects, all information presented during the diagnosis stage should be brief and basic accompanied by assurance and support.

All diet instructions should be preceded by an extensive interview of the patient. Information obtained during this informal discussion will include his usual meal and snack times, food preferences, methods of food preparation used in the home and the amount of physical activity in his daily schedule. Using these facts, the dietitian can plan a meal plan that will coincide with the action of his insulin and yet allow him to retain some of his former eating habits.[3]

Ideally, the diet as taught in the hospital will include only the information necessary for the patient to plan his meals at home. He should become familiar with the exchange lists and their use in meal planning, prevention of hypoglycemic reactions, and adjustment of food intake for increased activity. More extensive instructions will be included in the indepth class they attend at a later date. Some patients will find it impossible to attend such a class, so it is wise to include printed information on restaurant eating, meal planning during illness, and cookbook suggestions so the patient may refer to it as needed.

Once the patient has received his own meal plan and the exchange lists, he should be encouraged to select his meals from the hospital menu. The dietitian must make any necessary corrections before meals are served. In this way, the patient will become familiar with the exchange lists and the dietitian can evaluate his understanding of the diet.

There are a variety of teaching methods and aides suitable for educating the patient in his diet. Group sessions are beneficial as a setting for explaining the basics of meal planning. This saves the time of the dietitian and may also be an opportunity for some group interaction. In some hospitals such a class is part of a structured program; where this is not practical, classes can be held as necessary to meet the needs of the patients. Such group instructions must be followed by daily individual visits from the dietitian to answer questions and ensure the patient's thorough understanding of his regimen.

Many hospitals have incorporated in-patient and out-patient diabetes education programs into their services. Again, the team all shares in the responsibility of educating the patient but the education is of a more formal nature than the one-to-one informal method of education. The efficacy of educating groups with the same immediate concerns cannot be denied.

When the patients leave the hospital, they should be able to demonstrate competence in the basic tasks of diabetes management; i.e., proper administration of medication, urine testing, and meal planning. They should also have a grasp of the basic nature of diabetes and the prevention and control of the acute complications of acidosis and hypoglycemia. Reading material should be given to reinforce the teaching done in the hospital. Phone numbers of the community diabetes associations and of the physician, nurse and dietitian should be given so the questions that come up over the first few days at home can be answered quickly and factually.

After the patients have been home and managing their diabetes from four to six weeks, an indepth education course in the care and management of diabetes mellitus can be of tremendous benefit. After having the day to day experience of managing their diabetes, they are much better equipped to ask questions pertinent to their needs and their anxiety levels are usually decreased to a point that further education is now feasible. The Diabetes Education Center in Minneapolis offers such a course. The Diabetes Education Center's course is highly individualized and employs a variety of teaching methods including one-to-one, small group and formal classroom instruction. Topics include a review of basic management principles and then progresses on to more detailed topics such as long-term complications, pattern control, psychological adjustment, meal planning for special occasions and restaurant meal planning. Physician-patient consultations are done on a daily basis as well as individual sessions with the nurse and dietitian. A detailed letter is sent back to the patient's physician stating what changes were made in the management of the diabetes and recommendations for future care. Nursing and dietary consultations are available after the patient has completed the course. Similar Diabetes Education Programs are available in other areas of the state. Contact the American Diabetes Association of Minnesota office for programs in your area.

Education of the diabetic patient must not end with the formal in-patient and/or out-patient program. Office visits are a time when basic information and skills can be reviewed, new information can be imparted and built upon from visit to visit. Public health nurses can be an excellent resource for enhancing information in the home setting.

Who Can Teach the Patient?

The best approach in teaching the diabetic patient is the team approach utilizing the training and expertise of each member of the team to its greatest potential in the education process. The primary teaching team is the physician, nurse and dietitian. Other health care professionals such as the pharmacist, social worker and physical therapist can also be a part of the team.[4]

For a quality diabetes education program, the members of the teaching team must not only be knowledgeable in the field of diabetes care and management but also in patient education techniques.[5] The educator should have skills in communications, interpersonal relations, psychosocial adaptations, interviewing, assessment, teaching-learning techniques, evaluation, and use of audio-visual materials. The Health Education for Living Program and its Diabetes Education Center component in Minneapolis offers ongoing training programs for health professionals not only in diabetes but also in patient education techniques and methods of developing patient education programs.

Patient Involvement

The most important person in the health care team is the diabetic patient. He must be his own physician, nurse, dietitian, pharmacist, physical therapist, social worker and lab technician 365 days of the year. Educating the patient about his diabetes and his role in managing it is a key factor in equipping him for this responsibility.[6] Quality health care can only be achieved by informed patients cooperating with interested and knowledgeable health professionals.

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Arnold Lazarow, M.D., Ph.D.

(1916-1975)

Writing about a well-known figure in the scientific and professional world tends to become stilted and pedantic, dutifully noting dates, degrees, societies, honors and achievements in a catalogue fashion. The human, the personal, the essential elements have a tendency to become thin and almost vanishing. I should like to present to you a series of glimpses of Arnold Lazarow as we knew him.

The year is 1940 and in Professor Bensley's laboratory at the University of Chicago, a young graduate student, energetic, voluble, and good natured has joined the group that was using elegant centrifuge techniques to separate cell constituents. One of the granules turned out to be a glycogen protein complex—particulate glycogen. This finding and the long-standing interest of that laboratory in the islets of Langerhans determined the future work of Arnold Lazarow—endocrine control of carbohydrate metabolism, insulin synthesis and the care and feeding of B-cells.

During the second World War, Dunn and McLetchie discovered the lethal effects of alloxan on the B-cell. It was thus natural for Lazarow to devote himself and his group at Western Reserve to a study of the mechanisms of damage and the concept of—SH effects (glutathione) as a factor in the integrity of B cell membranes. Evident were the same work intensity, good nature and shared enthusiasm persisting into the professorial age period.

There are very few living creatures which have as grotesque a head as the teleost, goose-fish. Since this living fossil had islet-bodies separate from the enzyme producing pancreas, Arnold waited for them on the wharf at Woods Hole and took them to the laboratory so that the metabolism of the B cells and their insulin producing activity could be studied with as little damage as possible. The goose-fish were in his opinion beautiful, because they could provide answers to needed questions.

Arnold's thorough knowledge of the biology of the islet cells coupled with the available interest and expertise at the University of Minnesota in transplantation, provided the base and the push to the elegant studies on islet transplantation of the last years of his productive life. Again the same enthusiasm, the sharing and the hard work.

Somehow in between these work periods, Arnold served the Diabetes Associations (local and national) with advice and concern; established the most useful Diabetes Literature Index; edited symposia and chaired conferences; and evidently and clearly basked in harmony and relish within his family; with Jane and their two sons.

This is how we saw the man. The dry data follow as recorded in the American Men and Women of Science (1975 edition) p 563, 197:

> Lazarow, Arnold, b Detroit, Mich. Aug 3, 16; m 40; c 2. Anatomy, Cell Biology. Educ: Univ Chicago, BS, 37, MD, 41, PhD (exp endocrinol, cytochem, anat) 41. Prof Exp: Res assoc, Univ Southern Calif, 43; sr instr anat, Western Reserve Univ, 43-46, from asst prof to assoc prof, 46-54: Prof and Head Dept, Med Sch, Univ Minn, Minneapolis, 54-concurrent Pos: Spec consult, USPHS; trustee, Minn Med Found, 57-65, pres, 60-62; trustee, Marine Biol Lab, 61-; vis lectr, Univ Dundee, 63; mem nat adv coun, Nat Inst Arthritis & Metab Dis, 61-65; mem coun arteriosclerosis, Am Heart Asn Honors & Awards: Capps Prize, 42; Banting Medal, Am Diabetes Asn, 73. Mil Serv: Civilian with Off Sci Res & Develop, 41. Mem: Am Chem Soc; Soc Exp Biol & Med; Soc Gen Physiol; Histochem Soc (pres, 65-66); Am Asn Anat. Am Diabetes Asn. Res: Separation of cell components; localization of enzymes in cell components; mechanisms of Janus green B staining reaction of mitochondria; islet organ culture and transplantation; experimental diabetes; glutathione protection against diabetes; studies on isolated islet tissue of fish; microanalytical techniques; insulin biosynthesis and secretion; information retrieval. Add: Dept of Anat Univ of Minn Med Sch Minneapolis MN 55455.

Rachmiel Levine, M.D.
Executive Medical Director
City of Hope Medical Center
Duarte, California

Editorials

Diabetes Mellitus—1976

The magnitude of the problem of diabetes mellitus is brought to one's awareness not only by the frequent reference to the 10 million people afflicted by this disorder in the United States[1] or by the many examples of chronic complications observed in the practice of medicine, but also by the frightening experiences described by many young, healthy, intelligent diabetics who have experienced an incapacitating bout of hypoglycemia as the result of their treatment.

Clinical and basic research in the field of diabetes in the past 10 to 15 years has greatly enhanced our understanding of the pathophysiology of diabetes and the genesis of its chronic complications. We can now state that the relationship of the genesis of the chronic complications of diabetes mellitus to the metabolic abnormalities is established[2] and the evidence that maintenance of normal blood glucose levels as many hours as possible each day prevents or delays the complications is mounting rapidly.[3-4] Even more exciting is the clear and unequivocal demonstration by Mauer, et al. as presented at the 36th annual meeting of the American Diabetes Association in San Francisco, June 1976, that the changes of diabetic nephropathy (in animals) are clearly *reversible* if a proper metabolic environment can be provided.

This knowledge no longer allows the physician caring for the diabetic patient to accept suboptimal control of the patient's diabetes. It is now our clear mandate to see that each of our diabetic patients are kept as near euglycemic at all times as is possible in the individual case.

The emphasis of the diabetologist must now shift to providing the primary care physician with all the information and support necessary to achieve the goal of optimum control in each patient. Major medical centers around the world have taken such differing approaches to the treatment of diabetes mellitus in the past that confusion has resulted even in the minds of the most sophisticated diabetologists, let alone the family physician who is making a sincere effort to treat the disease to the best of his ability. One virtue of these varied programs is that, with the passage of time, some have been shown clearly to be superior to others. Diabetologists must now make a sincere effort to determine the optimal, eliminating the confusing variety of sub-optimal programs in current use in favor of a more effective and uniform approach, always taking advantage of the true advances in management of diabetes mellitus as they occur. Advances in diabetes research are exciting, occurring regularly, and nicely outlined in this issue by Dr. F. C. Goetz.*

Despite these advances, two things remain obvious. The first is that currently available methods of treating diabetes mellitus remain the backbone of therapy, and will for at least the next decade. Equally obvious is that our improved understanding of the pathophysiology of diabetes and the genesis of its chronic complications can lead to a more optimal utilization of the presently available forms of therapy to the ultimate benefit of our diabetic patient. Especially important is the concept that timing of insulin action must correspond to the time of glucose presence.[5] Insulin treatment programs based on this maxim are considered optimal. When combined with intensive education of the diabetic patient so that he can manage his problem correctly, making the proper adjustments in his program from day-to-day as problems arise, rather than from physician visit-to-physician visit, the treatment of diabetes mellitus can indeed be effective and the long-term prognosis improved.

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*See page 779.

The American Diabetes Association of Minnesota is especially pleased to co-sponsor this issue of MINNESOTA MEDICINE during this National Diabetes Month. Included in this issue is current information clinically useful in the management of the problems of the patients with diabetes mellitus.

G. E. Cotton, M.D.*
Guest Editor

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*Vice-President for Professional Education, American Diabetes Association, Minnesota and Assistant Professor of the Clinical Sciences, University of Minnesota Medical School-Duluth.

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Help Your Diabetic Patients

Make Them Aware of ADAM

THE AMERICAN DIABETES ASSOCIATION OF MINNESOTA, INC. (ADAM) was incorporated June 1, 1974. With the help of many volunteers, related organizations, and a dedicated staff, its growth since that date has been tremendous. ADAM today has three chapters and 21 units.

When ADAM was founded, its stated objectives were to further the general welfare and to undertake in the public interest such activities as will improve the well-being of persons having diabetes mellitus. To these ends the purposes of ADAM are:

> To develop educational methods designed to give those who have diabetes mellitus a better understanding of their condition;
> To promote among health professionals and others the free exchange of knowledge with respect to diabetes mellitus; to improve the standards of treatment of diabetes mellitus;
> To disseminate accurate information about diabetes mellitus to the general public, to educate the public in the importance of early recognition of diabetes mellitus and of medical supervision of its treatment;
> To promote research related to diabetes mellitus by individuals, hospitals, clinics, universities and other institutions or organizations.

A brief history of ADAM tells some of the story of its growth. The Twin Cities Diabetes Association, Inc. (TCDA) was incorporated in 1948 to serve the people with diabetes mellitus in the Twin City area. As its excellent reputation in the metropolitan area spread throughout the State of Minnesota TCDA was asked to provide its services to outstate groups. This was not possible because the majority of its funds came from the United Ways of Minneapolis and St. Paul and the expenditure of those funds was restricted to the Metropolitan area. To fulfill this outstate need, ADAM was organized in June of 1974.

Starting with nothing more than a group of willing volunteers and the superb cooperation of the staff of TCDA, ADAM began to make itself known throughout the State of Minnesota. In April, 1975, ADAM hired an executive director as its first staff member to "put the show on the road." Evidence of this accomplishment is the number of chapters and units presently on board.

Another significant happening in the history of ADAM occurred when the Diabetes Research Fund, Inc. (DRF) was incorporated in January, 1973. DRF was organized by a group of people, principally parents of diabetic children, who were interested in raising funds for research in diabetes. These highly enthusiastic volunteers raised over $400,000 for research in a two and one-half year period. DRF started a national Christmas card campaign which is expected to raise $150,000 for nationally distributed diabetes research for the year 1976. In order to avoid duplication of effort and to present a unified front throughout the State of Minnesota, DRF merged with ADAM on June 28, 1975.

To achieve its four priorities of professional education, public information, patient education, and research, ADAM provides comprehensive programing in these areas. Each year three major professional symposia are held in various regions of the state, designed to update physicians, nurses, and dietitians, and to assist them in staying current with new developments in the field of diabetes mellitus. Each year ADAM produces a television series of twenty-six one-half hour programs entitled "The Diabetic Today." This program deals with the broad spectrum of education for the diabetic and his family. ADAM chapters and units throughout the State of Minnesota hold regular monthly educational meetings. These and many other programs are reasons why diabetics all over the state should be encouraged to become active in their local diabetes chapter or unit.

Today, ADAM is the Minnesota affiliate of the American Diabetes Association, Inc., the national organization. ADAM is a legally registered non-profit, tax exempt, 501 (c) (3) organization and is approved by the Minnesota Charities Review Council.

With the help of many people interested in improving the well-being of persons having diabetes mellitus, the American Diabetes Association of Minnesota is today one of the leaders in the country in the fight against diabetes mellitus. ADAM needs all help possible, both volunteers and monetary help, to continue this fight until someday we can say "We are out of business; the cure for diabetes has been found." We have included the names and addresses of all of our chapters and units.* Please contact any one of them to do your part in bringing the day of the cure that much closer.

Donald R. Moberg
President
American Diabetes Association of Minnesota

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*See page 806.

Management of the Pregnant Diabetic

THE ARTICLE OF Coniff and Maeder* is a good review of the changes and risks involved in the management of the pregnant diabetic. Early in the article it states that "when conception occurs the pregnant diabetic should search for good medical care usually in a team setting using facilities that most often can be provided at a regional perinatal center."

The recommendations of the committee on regionalization of health care delivery for obstetrics places diabetes mellitus Class B-F as a predisposing high risk medical factor which would indicate appropriate consultation and delivery at a Level II or Level III center. The reason for this suggestion can be noted from seeing the list of complications of diabetes found in Table 2 in their article. One of the factors which is alluded to in the timing and method of delivery is the use of serial esteriol determinations and oxytocin challenge testing to determine the quality of placental function. Because these tests are expensive and are not readily available in many areas the diabetic should be in a center where these tests can be done and the timing of pregnancy so set to avoid a stillborn.

It must be clear to all who manage a pregnant diabetic that they are dealing with a high risk patient. Diabetes and pregnancy in combination requires the best possible care since the number of pregnancies for diabetic patients may be limited. The management plan as found in Table 3 is a good general plan and should be carried out at a center which is able to take care of complicated pregnancies and high risk new born infants, since the infant of a diabetc docs require special neonatal care.

Peter E. Fehr, M.D.
Minneapolis, Minnesota

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*See page 772.

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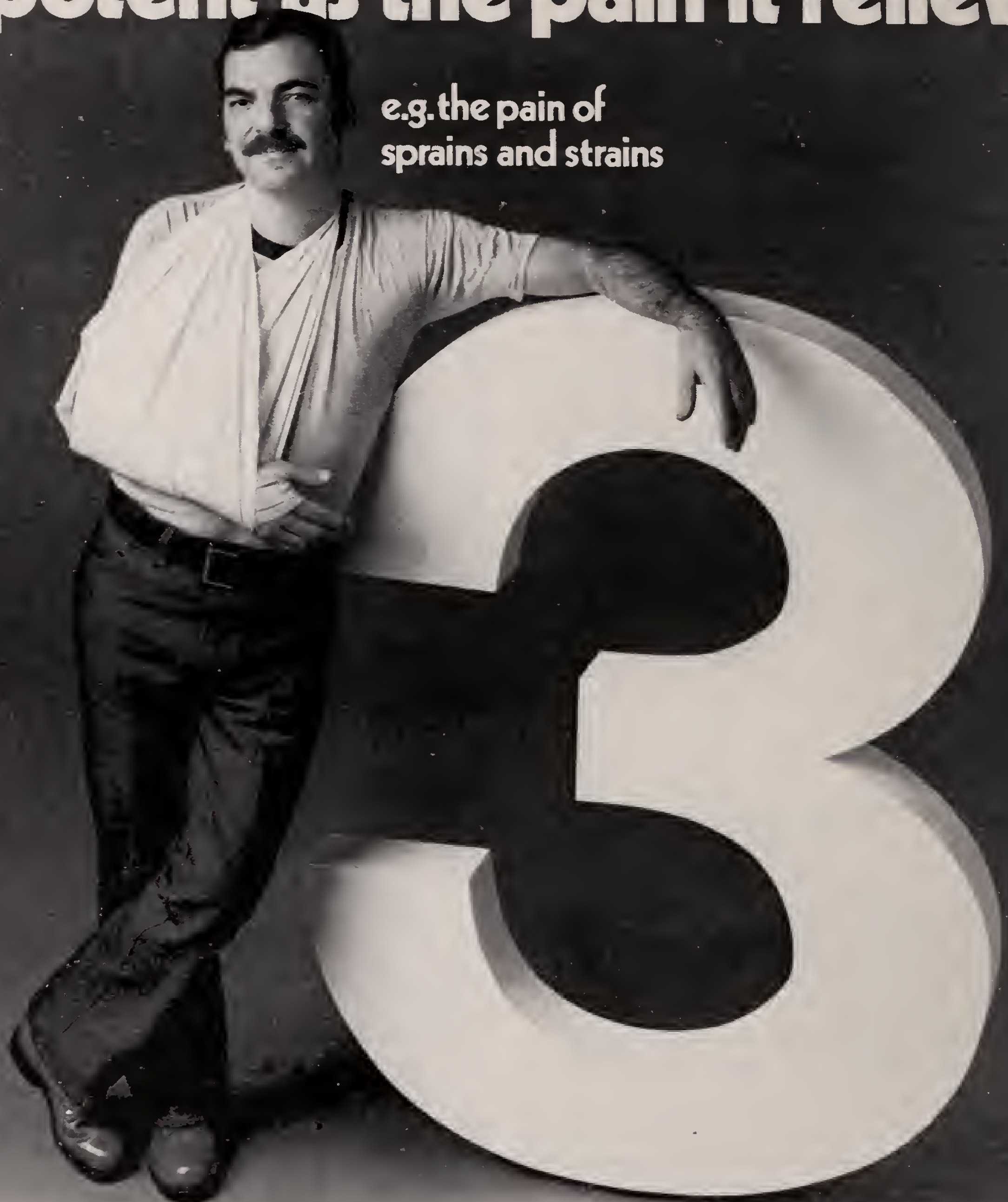

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Blood Glucose Control in Diabetes*

This policy statement of the American Diabetes Association is intended to publicize the belief that the weight of evidence, particularly that accumulated in the past five years,[1] strongly supports the concept that the microvascular complications of diabetes are decreased by reduction of blood glucose concentrations.

For almost 50 years, since insulin therapy was initiated, proponents of "rigid," "tight," or "chemical" control quoted retrospective evidence of decreased or delayed nephropathy and retinopathy as glucose levels are brought by therapy toward the normal range. Opponents to this hypothesis pointed to the problems of complications in many of these supposedly better-controlled patients, to the emotional and socioeconomic conflicts which often resulted from the demands of rigorous control, to the frequent difficulties with hypoglycemic reactions, and, recently, to the University Group Diabetes Project.[2,3]

Five years ago, in a review of 300 reports in the world literature evaluating control, Knowles[4,5] found data from 85 centers which were satisfactory for analysis. There were no prospective studies which proved or disproved that control prevented complications, and definite studies had yet to be done. He concluded that better means must be developed to achieve control than those presently available.

The University Group Diabetes Project was initiated to help settle the controversy. The five forms of therapy failed to demonstrate any effect upon microvascular lesions.[2,3] The middle-aged or older subjects studied exhibited only minimal initial hyperglycemia, however, and the reduction in blood glucose was small, so the results are not directly pertinent to the relationships between glucose levels and microvascular lesions.

In the past few years, numerous studies in animals, including dogs, rats, monkeys, Chinese hamsters, mice, and others, have demonstrated that reduction of hyperglycemia by insulin therapy, by transplantation of insulin-producing tissues, or by other means, prevents or minimizes formation of diabetic-like lesions in eye, kidney, and nerve.[1] Biochemical studies have shown persistent hyperglycemia to be associated with accumulation of sorbitol in nerve, eye, and vascular tissue and with alterations in vascular basement membrane.[6] Most recently, even hemoglobin has been found altered in man and experimental animals in the presence of persistent and prolonged hyperglycemia.[7-11]

Biopsies of kidney (and in some studies of muscle) have failed to show abnormalities for the first few years of insulin-dependent diabetes in man,[12-14] excluding thereby an independently inherited phenomenon. In a small but prospective study of randomly assigned patients just reported from Paris,[15] enthusiastically well-controlled diabetic subjects showed less retinopathy. Thus, the contention that the microvascular complications occur independently of the hyperglycemia and insulin deficiency and that control of the metabolic events is not a factor in their progress does not appear tenable any longer.

These data therefore place the burden of proof upon those who maintain that diabetes control is without effect. The goals of appropriate therapy should thus include a serious effort to achieve levels of blood glucose as close to those in the nondiabetic as feasible. Obviously, patient needs and resources must also be carefully assessed and the goals individualized accordingly. This concept is particularly applicable to the diabetics at greatest risk of developing the microvascular complications—the young and the middle-aged. It is well appreciated, however, that in some juvenile-onset-type subjects, it is most difficult, even with multiple insulin injections, to achieve any significant degree of control of the hyperglycemia. Also, in certain elderly patients, the shorter life expectancy may preclude the need for achieving lower glucose levels, providing they are asymptomatic.

In summary, current clinical and experimental data clearly demonstrate that optimal regulation of glucose levels should be achieved in the treatment of diabetes, particularly in young and middle-aged individuals, who are at greatest risk

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*Reprinted from Diabetes 25:3, March 1976. By permission.

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It can be concluded that current means of therapy are only partly effective at best, and therefore a high priority must be assigned to the development of more physiologic insulin delivery systems or to approaches to the correction of the deficient insulin-producing mechanism itself. Finally, good diabetic management necessitates education and training of both patients and health professionals in the technics involved, and close coordination and cooperation in patient management. Most important is a commitment to the view that better "control," when achievable, is beneficial.

American Diabetes Association
George F. Cahill, Jr., M.D., President
Donnell D. Etzwiler, M.D., President-Elect
Norbert Freinkel, M.D., Vice-President: Professional Section

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Children's Health Center of Minneapolis

First Annual Philip A. Rierson Memorial Lecture
Tuesday, November 9, 1976
The Campus Club
Coffman Memorial Union

6:00 p.m. Reception
7:00 p.m. Dinner
8:00 p.m. Rierson Memorial Lecture, Mayo Memorial Auditorium

Guest Speaker: Norman Jaffe, M.D., Chief Pediatric Solid Tumor Service, Sidney Farber Cancer Institute, Boston, Massachusetts. "Current Concepts in the Management of Pediatric Malignancies with Prospects for the Future."

Program Courtesy of Mead Johnson Laboratories. Contact: Karen Olness, M.D., Children's Health Center, 2525 Chicago Ave. So., Minneapolis, MN 55404.

Refer to this listing for the Diabetes group nearest you
Minnesota State Office

American Diabetes Association of Minnesota
T. Harrison Bryant, Executive Director
7601 Bush Lake Road
Minneapolis, Minnesota 55435
612-835-2800

Chapters

Twin Cities Diabetes Association
Donna Fillmer
6490 Excelsior Blvd.
612-927-4487
W-414 Meadowbrook Building
St. Louis Park, Minnesota 55426

Duluth Diabetes Association
Miller-Dwan Hospital
504 East 2nd Street
Duluth, Minnesota 55802
or contact
Marcy Siddall
218-624-1746

Rochester Diabetes Association
Vera Mae (Bobbi) Darr
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Rochester, Minnesota 55901
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Units

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Austin, Minnesota 55912
work—507-437-5611
home—507-433-5754

Bemidji Diabetes Association
Neen Lillquist
214 Birch Hall
Bemidji, Minnesota 56601
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Blue Earth-Nicollet County (Mankato)
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Hibbing Association
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Hibbing General Hospital
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Hibbing, Minnesota 55746
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MINNESOTA MEDICINE

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Farrell Stiegler, M.D.
Cover Editor

MSMA Highlights

1976 MSMA Socio-Economic Conference

Senator John G. Tower, (U.S. Senate, R-Texas)

Joseph P. Newhouse, Ph.D.

Essential information for the Minnesota physician practicing in today's socio-economic environment . . . this is the 1976 Socio-Economic Conference. The first such meeting held by the Minnesota State Medical Association.

The Conference is scheduled to begin with a reception and dinner on Thursday evening (November 18) in the Thunderbird Motel, Bloomington, Minnesota. It concludes the next day (November 19) at noon and just prior to the opening of the MSMA House of Delegates at the Registry Hotel.

The Socio-Economic Conference is a **must** for physician leaders in Minnesota to prepare for the critical issues facing the profession in 1977.

The program features outstanding speakers such as: U.S. Senator John G. Tower of Texas and Rand Corporation medical economist, Joseph P. Newhouse, Ph.D.

Breakout sessions zero in on state legislation, health planning and third party reimbursement and relationships. Panels include the Speaker of the Minnesota House of Representatives, Martin O. Sabo, state and national experts on health planning, health insurance executives, and key representatives of Minnesota regulatory agencies.

The Socio-Economic Conference places emphasis on socio-economic information that the physician can use. Questions such as:

- How does the new Federal Health Planning Act (P.L. 93-641) affect the physician and his or her practice?
- What specialties are the first to be affected by the consumer dominated health planning boards?
- What rights can the physician demand in the health planning process?
- What health legislation enacted in the 1976 legislature will affect physician practice?
- What professional liability legislation was enacted in the last legislature and what are the prospects for remedial legislation in this key area during the 1977 session?
- What can the profession expect from the 1977 legislature when it convenes in January?
- What is a realistic appraisal of Minnesota physicians' relationship with Blue Cross/Blue Shield?

What problems have been solved and what issues are unresolved in this relationship?

- The physicians' relationship with Medicaid and specifically how the physician should relate to the Department of Public Welfare and the entire Medicaid process.

These and other key issues will be raised during the Socio-Economic Conference.

The program format has been planned to allow maximum participation. Since it precedes the opening of the House of Delegates on Friday afternoon, November 19, the Conference offers a convenient way for many physicians and their wives to attend before the House opens.

MSMA Annual Socio-Economic Conference
November 18-19, 1976
Thunderbird Motel, Bloomington, Minnesota

Thursday, November 18, 1976

6:30- 7:30 p.m. Early bird cocktail reception
7:30 Dinner
Speaker: Senator John G. Tower (R. Texas)
Moderator: Chester A. Anderson, M.D., President-Elect
Minnesota State Medical Association

Friday, November 19, 1976

7:30 a.m. Breakfast with Joseph P. Newhouse, Ph.D.
Moderator: Robert W. Geist, M.D., President-Elect
Ramsey County Medical Society
8:30- 8:45 General Session
Socio-Economic Facts of Life for the Minnesota Physician
Speaker: Richard E. Anonsen, M.D., President
Minnesota State Medical Association
8:45- 9:00 Breakout Subject Introductions (Audio-Visual)
State Legislation
James H. Sova, Panel Moderator
Director, Department of Legislative Affairs, MSMA
Chester A. Anderson, M.D.
President-Elect, MSMA
Chairman, MSMA Committee on Legislation
Martin O. Sabo, Speaker
Minnesota House of Representatives
Mr. John Krichbaum
Department of Legislation, AMA
Richard L. Engwall, M.D.
Chairman, MINNPAC Board of Directors
Health Planning
Thomas P. Galligan, Panel Moderator
Director, Department of Health Planning, MSMA
John B. Coleman, M.D.
Chairman, MSMA Committee on Health Planning
Mr. John Dilley
Director, Minnesota Health Planning Agency
Mr. Malcolm Mitchell
Director, Metropolitan Health Board
Health Systems Agency 5
Carlton Erickson, M.D.
HSA Physician Chairman

Friday, November 19 (Continued)

Health Delivery & Third Party Relationships

Lois J. Wilzewske, Panel Moderator
Director, Department of Socio-Economic Research, MSMA
Martin Van Herik, M.D.
Chairman, MSMA Committee on Medical Service
Mr. James Hiniker
Deputy Commissioner, Minnesota Department of Public Welfare
Mr. James Regnier
President, Minnesota Blue Cross/Blue Shield
Mr. William Lanzo
Travelers Insurance

9:00- 9:45 Breakout Session #1
9:50-10:35 Breakout Session #2
10:40-11:25 Breakout Session #3
11:30-12:00 General Session—Moderators of Breakout Sessions in a Dialogue with:
Mr. Bernard P. Harrison
Group Vice President, External Affairs
American Medical Association
Moderator: Richard J. Frey, M.D., Chairman
Minnesota State Medical Association Council

MSMA Annual Socio-Economic Conference Registration
Thunderbird Motel, Bloomington, Minnesota
November 18 & 19, 1976

CONFERENCE RECEPTION & DINNER—Thursday, November 18, 6:30 P.M.
CONFERENCE BREAKFAST & PROGRAM—Friday, November 19, 7:30 A.M.

Registration Price: $25 (includes all meals and conference materials) Number of tickets ....

ALL TICKETS WILL BE HELD AT THE REGISTRATION DESK.
ADDITIONAL TICKETS WILL BE ON SALE AT THE REGISTRATION DESK.

Please make checks payable to MSMA and return check with this page to: Minnesota State Medical Association, Socio-Economic Conference, 101 East 5th Street, Suite 900, St. Paul, MN 55101.

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When? November 19 & 20, 1976
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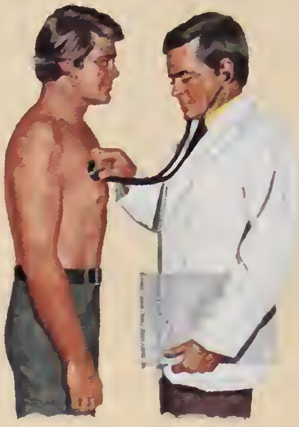
Narrowing down pneumonias

Upjohn

Bacterial or nonbacterial?

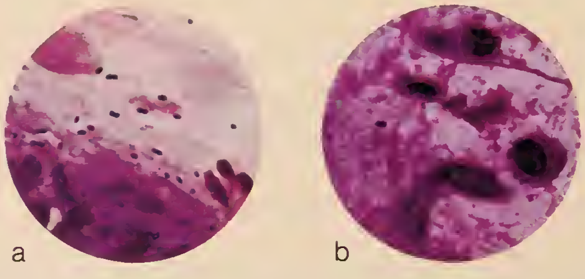
In the early stages of mild to moderate pneumonia, it is often difficult to reach an accurate bacteriologic diagnosis. A tentative differentiation may be made on history-taking, physical examination, CBC with differential analysis, and microscopic study of the sputum smear. Specimens should be obtained for culture and sensitivity testing, but when a bacterial pneumonia is diagnosed, therapy is often instituted before the etiological agent is positively identified.



Bacterial pneumonias may have a sudden onset with a shaking chill, rapid development of fever, pleuritic pain, and cough productive of rust-colored sputum. The Gram-stained sputum smear generally shows polymorphonuclear neutrophils as well as a predominance of the causative organisms. These are likely to be *Streptococcus pneumoniae,* still by far the most frequently encountered agent in bacterial pneumonia.[1] The CBC reveals marked leukocytosis with a shift to the left.

In *nonbacterial pneumonias*—mycoplasmal or viral—classical symptoms tend to develop more slowly, with myalgia, lassitude, and headache predominating. Sputum production is usually scanty, and the sputum smear is relatively uninformative, showing gram-positive cocci and other organisms which are part of the normal pharyngeal flora. The leukocyte count is normal or slightly elevated.

Direct Gram-stained sputum smears. (a) Pneumococcal pneumonia—note abundant polymorphonuclear leukocytes, as well as gram-positive diplococci. (b) Nonspecific—consistent with viral or mycoplasmal pneumonia. Note large mononuclear cell, as well as a few polymorphs and mixed bacterial flora (pharyngeal contaminants).

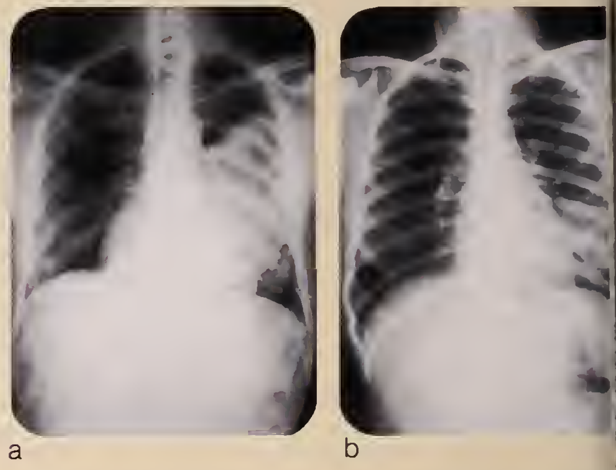


Mycoplasmal or viral?

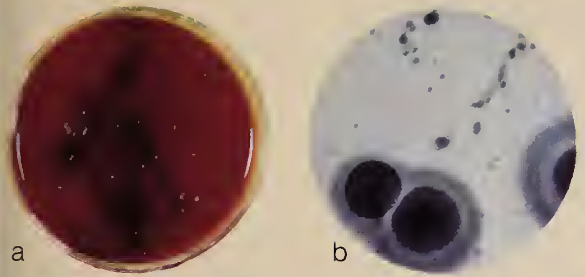
Differentiation between mycoplasmal and viral pneumonias may be impossible in the acute stag

Serologic testing and culture methods for *Mycoplasma pneumoniae* are complex and time-consuming, taking as long as two weeks after obtaining samples. The sensitivity and specificity the test for cold agglutinins have been questione The complement-fixing antibody test may reflect previous infection. Furthermore, facilities for cultu *M. pneumoniae* are not widely available.[3]

If treatment is to be initiated, therefore, it may necessary to start on the basis of a *presumptive* diagnosis of mycoplasmal pneumonia.[1-3] In reach such a diagnosis, the physician relies on clinical judgment, considering such factors as the age of patient and the history of exposure. For example, *Mycoplasma pneumoniae* is considered the most common cause of pneumonia among ambulatory patients aged 20 to 35.[1]



Chest x-rays of patients with (a) pneumococcal pneumonia—classically heavy, extensive infiltration of left lung, (b) mycoplasmal pneumonia—mild infiltrate confined to left lower lobe. Roentgenography usually does not help in differential diagnosis, since both types of pneumonias may present with a wide spectrum of x-ray as well as clinical findings.



(a) Distinct mucoid colonies of type 3 pneumococci *(Streptococcus pneumoniae)* on sheep blood agar showing greenish discoloration (alpha-hemolysis) of medium. (b) Typical "fried-egg" colonies of *Mycoplasma pneumoniae* consisting of dense central core with lighter periphery. Cultural and serologic methods for detecting *M. pneumoniae* are complex, time-consuming, and not widely available.

Expectant therapy

he patient with a presumptive diagnosis of coplasmal pneumonia or bacterial pneumonia, it y be desirable to initiate antibiotic therapy before lture and sensitivity results are available.

A course of erythromycin or tetracycline is nsidered effective in the treatment of mycoplasmal eumonia to help speed the clearing of infiltrate and orten the duration of symptoms.[1,3] In pneumococcal eumonia, erythromycin is an effective alternative to nicillin, the drug of choice. A recent report, based data from 200 hospitals of 100 beds or more, found % of *S. pneumoniae* sensitive *in vitro* to thromycin.[4]

Among these therapeutic agents, only thromycin provides effective coverage of both *coplasma pneumoniae* and *S. pneumoniae*. The nicillins are not effective against *Mycoplasma*, and *neumoniae* has shown a relatively high incidence esistance to tetracycline.

When erythromycin is selected for therapy, Mycin (erythromycin enteric-coated tablets, Upjohn) good choice. E-Mycin is administered and sorbed as active erythromycin base, and may be en q.i.d., q 6h, or b.i.d., immediately after meals or tween meals. Thus, patients can use mealtimes to p them remember their medication. The enteric ating on E-Mycin tablets helps ensure efficient sorption in the intestinal tract, and bioavailability dies show that E-Mycin can be expected to duce predictable, acceptable blood levels. The cost of E-Mycin helps assure economical therapy.

E-Mycin rarely causes serious side effects and is associated with liver toxicity.* The most frequent e effects are upper gastrointestinal, such as dominal cramping and discomfort, and are dose-ated. Nausea, vomiting, and diarrhea occur equently with usual oral doses. Serious allergic ctions, including anaphylaxis, have rarely been orted.

cautiously in patients with severe liver impairment

ERENCES: **1.** Chusid EL, Dalrymple W, Holloway WJ, et al: Managing the infectious umonias. *Patient Care* 9 122-167, 1975. **2.** The occasional might of mycoplasma. *rgency Med* 7:82, 85, 1975 **3.** Stevens DA. Viral and Mycoplasma pneumonias. *grad Med* 55:81-86, 1974 **4.** Data source: PMR Bacteriologic Report, Winter Series

Summary

Because pneumonias may be difficult to differentiate at the outset, treatment is often initiated before a causal diagnosis is made. However, readily available diagnostic criteria occasionally allow early differentiation between bacterial and nonbacterial pneumonias. When the diagnosis appears to be nonbacterial pneumonia, further differentiation between mycoplasmal pneumonia and viral pneumonia is more complex and time-consuming. Therefore, therapy is often initiated on the basis of a *presumptive* diagnosis of mycoplasmal pneumonia.

Erythromycin is an effective antibiotic against *Mycoplasma pneumoniae, Streptococcus pneumoniae,*† and *Streptococcus pyogenes.*† E-Mycin (erythromycin enteric-coated tablets, Upjohn) is administered and well absorbed as the active base, may be taken immediately after meals or between meals, and is essentially nontoxic.

†Although penicillin remains the drug of choice against these organisms, erythromycin is an effective alternative

E-Mycin® 250 mg

erythromycin enteric-coated tablets, Upjohn

wide-ranging usefulness in pneumonia*

*Mild to moderately severe, due to susceptible organisms.

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1975-1976 Data are a compilation of laboratory reports submitted during December 1975 and January and February 1976 by 200 acute care hospitals of 100 beds or more

Please turn page for brief summary of prescribing information.

Wide-ranging usefulness in pneumonia*

E-Mycin® 250 mg

erythromycin enteric-coated
tablets, Upjohn

Upjohn

- For mild to moderately severe infections due to susceptible organisms that commonly invade the respiratory tract
- Essentially nontoxic (see Precautions and Adverse Reactions below)
- Documented bioavailability
- May be taken immediately after meals or between meals
- Active base formula produces predictable blood levels
- Formulated for quality...priced for economy

E-MYCIN® TABLETS — 250 mg — For Oral Administration (erythromycin enteric-coated tablets, Upjohn)
E-Mycin Tablets are specially coated to protect the contents from the inactivating effects of gastric acidity and to permit efficient absorption when administered either immediately after meals or when given between meals on an empty stomach.

Indications: *Streptococcus pyogenes (group A beta-hemolytic streptococci):* Upper and lower respiratory tract, skin, and soft-tissue infections of mild to moderate severity. Parenteral benzathine penicillin G is considered by the American Heart Association to be the drug of choice in the treatment and prevention of streptococcal pharyngitis and in long-term prophylaxis of rheumatic fever. When oral medication is necessary (because the parenteral route is contraindicated) or if there is known allergy to penicillin, the following recommendations made by the American Heart Association apply: 1) Oral penicillin G or V (where no allergy exists)—This is the drug of choice. Give for a minimum of 10 days; 2) Erythromycin—Give for a minimum of 10 days. A few strains of streptococci resistant to erythromycin have been reported.
Alpha-hemolytic streptococci (viridans group): Short-term prophylaxis against bacterial endocarditis prior to dental or other operative procedures in patients with a history of rheumatic fever or congenital heart disease who are hypersensitive to penicillin. (Erythromycin is not suitable prior to genitourinary surgery where the organisms likely to lead to bacteremia are gram-negative bacilli or the enterococcus group of streptococci.)
Staphylococcus aureus: Acute infections of skin and soft tissue of mild to moderate severity. Resistance may develop during treatment.
Diplococcus pneumoniae: Upper respiratory tract infections (eg, otitis media, pharyngitis) and lower respiratory tract infections (eg, pneumonia) of mild to moderate degree.
Mycoplasma pneumoniae (Eaton agent, PPLO): In the treatment of primary atypical pneumonia, when due to this organism.
Treponema pallidum: Infections due to this organism.
Corynebacterium diphtheriae and *Corynebacterium minutissimum:* As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers. In the tre ment of erythrasma.
Entamoeba histolytica: In the treatment of intestinal amebias only. Extraenteric amebiasis requires treatment with other agent
Listeria monocytogenes: Infections due to this organism.

Contraindication: Contraindicated in patients with known hype sensitivity to erythromycin.

Warning: Safety for use in pregnancy has not been establishe
Precautions: Erythromycin is principally excreted by the live Caution should be exercised in administering the antibiotic patients with impaired hepatic function. Surgical procedure should be performed when indicated.

Adverse reactions: The most frequent side effects of erythr mycin preparations are gastrointestinal, such as abdomin cramping and discomfort, and are dose-related. Nausea, vomi ing, and diarrhea occur infrequently with usual oral doses During prolonged or repeated therapy, there is a possibility overgrowth of nonsusceptible bacteria or fungi. If such infec tions occur, the drug should be discontinued and appropriat therapy instituted. Mild allergic reactions such as urticaria an other skin rashes have occurred. Serious allergic reactions, i cluding anaphylaxis, have been reported.

Treatment of overdosage: The drug is virtually nontoxic, thoug some individuals may exhibit gastric intolerance to even ther peutic amounts. Allergic reactions associated with acute ove dosage should be handled in the usual manner—that is, by th administration of adrenalin, corticosteroids, and antihistamine as indicated and the prompt elimination of unabsorbed drug in addition to all needed supportive measures.

How supplied: 250 mg enteric-coated tablets—in bottles of 100 an 500 tablets, and in unit-dose packages of 100 tablets. Caution Federal law prohibits dispensing without prescription.

For additional product information, consult the package inser or see your Upjohn Representative.
NAS-4

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*Mild to moderately severe, due to susceptible organisms

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Classified advertising rates are thirty (30) cents a word; minimum monthly charge $7.50; key number, $1.00 additional.

Replies to advertisements with key numbers should be mailed in care of Minnesota Medicine, 101 East 5th, Suite 900, St. Paul, Minn. 55101.

PRIMARY CARE—Physicians needed to care for ambulatory and inpatients in active 224 bed, JCAH approved, University affiliated hospital. Competitive salary. Liberal fringe benefits. 40-hour work week allows ample time to enjoy outstanding recreational, cultural opportunities available in this area. Call (701-232-3241) or write: Chief of Staff, VA Hospital, Fargo, North Dakota 58102.

170 ACRES ALL WOODED on State Highway in Dakota County, fastest growing community in State. Priced right, rising land values in this area. Will assure investor of a substantial profit. Call or write Frank Pessek, 303 Park Lane, So. St. Paul, Minn. Phone 455-4161.

FAMILY PRACTITIONER wanted to join corporate group of five physicians. Liberal fringe benefits: Profit sharing, health insurance, life and disability insurance, malpractice insurance. Medical building adjacent to 52 bed accredited hospital. Associated with University Medical School. College, two lakes, great fishing, hunting and water sports. Rapid growing community. South Eastern South Dakota. Population of 6600 serving area of 20,000. For complete details write or call: Terry T. Kass, The Madison Clinic, Ltd., 903 North Washington, Madison, South Dakota. 57042. Office: 605-256-4564. Home: 605-256-6212.

TWO CENTRAL MINNESOTA communities are seeking three to four family practice physicians to staff two clinics. Guaranteed $35,000 salary plus fringe. Access to a 360-bed hospital and multi-specialty referrals. Contact Dennis Kleinsausser, St. Joseph-Cold Spring-Area Medical Planning Council, 22 South 5 Avenue, St. Cloud, MN 56301. 612-251-7110.

OPHTHALMOLOGIST trained U of PA. ECFMG, FLEX in preparation. Married, children, 23 years experience in medical and surgical ophthalmology. Wants work in hospital, clinic or group. Prefer to be near but not necessarily in urban area. Mostly convenient for access of old own patients immigrating to Twin City area. Contact: Vinh Dan, M.D.; 580 E. Minnehaha Ave., Apt. 7, St. Paul, MN 55101. Phone (612) 776-7384.

BROWERVILLE, MINNESOTA needs two family physicians to help provide medical care to Central Todd County. Existing physician now needs help because of increased work load. Thirty-two bed J.C.A.H. accredited hospital with five year old clinic owned by the city which is second to none. A rural setting with plenty of hunting, fishing and golfing opportunities for your enjoyment and relaxation. If what we have to offer interests you contact: Dr. Russell T. Brown, Browerville, Minnesota 56438, or phone: (612) 594-2231 or 594-2931.

FAMILY PRACTICE PHYSICIAN—To join group of six GP's, General Surgeon, and Family Counselor. Immediate workload, effective call system, early corporate opportunity with excellent salary and fringe benefits. Well equipped new clinic with over 11,000 square feet, group located in expanding community of over 10,000 with excellent educational and recreational facilities, only 30 minutes from downtown Minneapolis. Fully accredited 116 bed hospital in community. Call collect or write D. R. Lynch, M.D. or D. C. Fleming, Clinic Administrator, phone (612) 445-1305, Shakopee Medical Center, 1335 E. 10th Av., Shakopee, MN 55379.

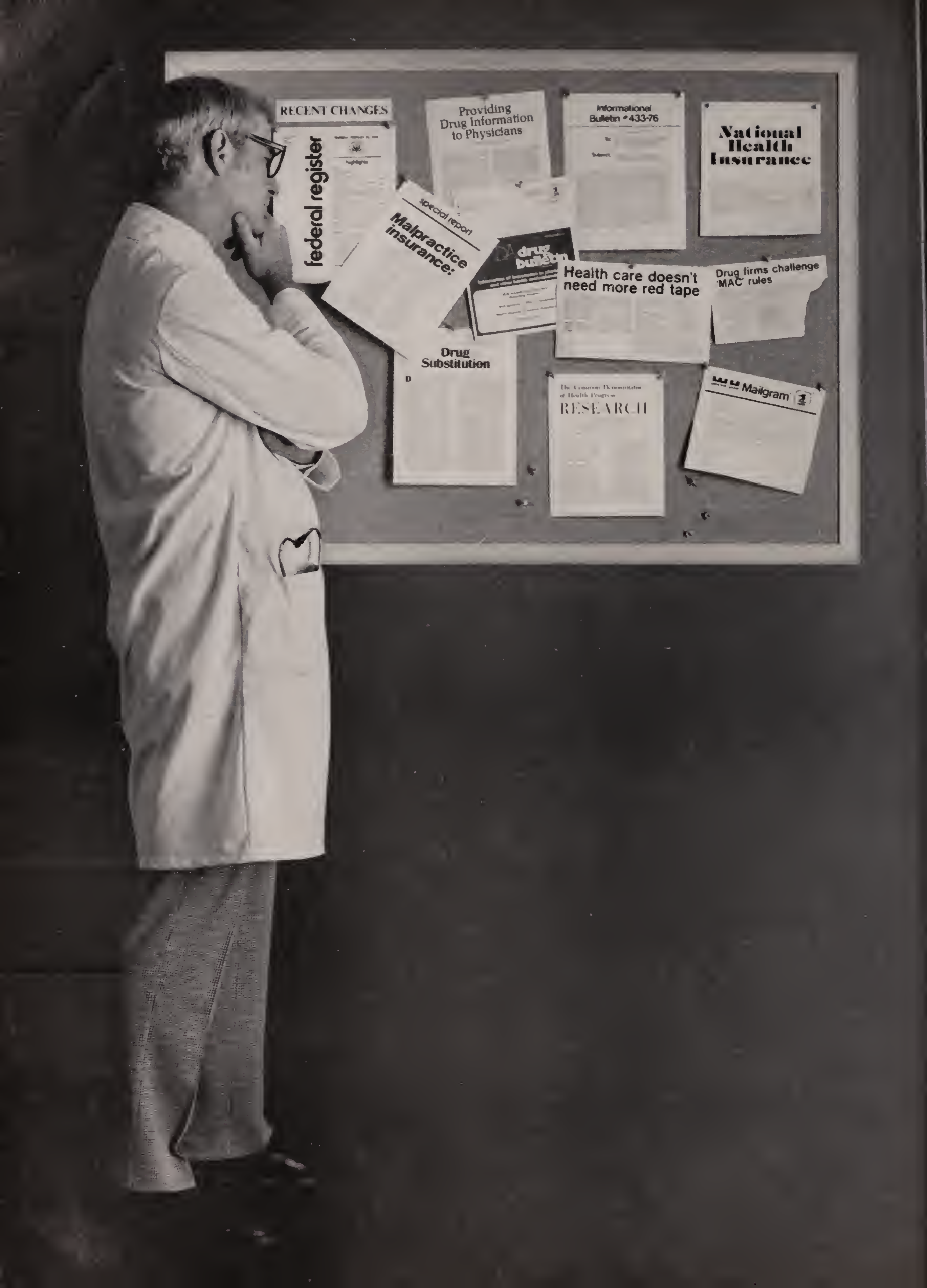
WANTED—Physician to join Clinic doing only Occupational Medicine, Physical Exams, Emergency and Minor Surgery. Two of the physicians are certified in Occupational Medicine, however, this is not required. Excellent hours, very little night or weekend work. Liberal fringe benefits. Contact L. B. Folsom, M.D., Northwest Industrial Clinic, P.A., 3033 University Ave. S.E., Minneapolis, Minn. 55414. Phone: 336-9353.

WANTED—FAMILY PHYSICIAN for clinical practice and curriculum development in expanding interdisciplinary rural health care program. Contact: Dr. John B. O'Leary, Dept. of Family Practice & Community Health, PO 227 Mayo, U of Mn Medical School, Mpls., 55455. Phone 612-376-3334.

FAMILY PRACTICE, INTERNAL MEDICINE, Obstets-Gynecology. The above physicians wanted in Southwestern Michigan. Clinic is located next to an 89 bed general Hospital, with excellent staff and equipment, provide high quality medical care. All members of the group are board certified or eligible. Excellent fringe benefits and starting salary. Please write or call: Gary Piippo, Administrator, Allegan Medical Clinic, P.C., 551 Linn St., Allegan, Michigan 49010. Phone: Area Code 616-673-8402.

VA HOSPITAL, ST. CLOUD, MINNESOTA has openings on its staff for a Psychiatrist, a General Practitioner, and an Internist. Consider, an employment situation which offers a 40-hour week, malpractice coverage, excellent fringe benefits, a competitive salary based upon qualifications, along with excellent nursing, social work, and psychology staffs which complete the treatment team; and, a quality of life which provides clean air, abundant outdoor recreation, and the opportunity to live in a city voted the "All-America" label in 1974. Three local colleges offer many cultural and educational advantages as does the city of Minneapolis which is only one hour away. License in any state accepted. Financial assistance in moving. Equal Opportunity Employer. Write or phone collect: Chief of Staff, VA Hospital, St. Cloud, Minnesota 56301; telephone (612) 252-1670, Extension 262.

(Continued on page 820)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THERE ARE A LOT OF PEOPLE GETTING BETWEEN YOU AND YOUR PATIENT.

Medicine today is in the spotlight, subjected to all inds of scrutiny. Your control over patient therapy is eing monitored, judged and occasionally abrogated, metimes by unknown third parties.

The worry is that in the wake of this focus, the relaionship between you and your patient will be weakened, ithout offsetting benefits. Consider three examples:

Drug substitution In most states, pharmacy laws, gulations or professional custom stipulate that your n-generic prescriptions be filled with the precise prodcts you prescribe. But in the last five years, a dozen or ore State laws have been changed, permitting the pharacist in most cases to select a product of the same neric drug to fill any prescription.

Ironically, this dilution of physician control has ken place against a background of growing evidence at purportedly equivalent drug products may be inuivalent, since neither present drug standards nor their forcement are optimal. In fact, the FDA itself says it s not enforced the same standards for hundreds of ollow-on" products that it had applied to the original DA approvals. Thus physician control over patient erapy is being eroded with a risk that patients may be posed to drugs of uncertain quality.

The major advertised claim for substitution is reduced escription prices for consumers. Yet no documentation any significant savings has been produced.

MAC Maximum Allowable Cost, MAC for short, is Federal regulation designed to cut the Government's ug bill by setting price ceilings for drugs dispensed to edicare and Medicaid patients. Unless the prescriber rtifies on the prescription that a particular product is edically necessary, the Government intends to pay only r the cost of the lowest-priced, purportedly-equivalent, generally-available product. The effect of the program may be that elderly and indigent patients will be restricted to products which someone in Washington believes are priced right. Practicing doctors will have little to say about administration of the program, since Government will have absolute authority to make its choices stick.

The drug lag The future of drug and device research depends upon a scientific and regulatory environment that encourages therapeutic innovations. The American pharmaceutical industry annually is spending more than $1 billion of its own funds and evaluating more than 1,200 investigational compounds in clinical research. Disease targets include cancer, atherosclerosis, viruses and central nervous system disorders, among others. But there is a major barrier to the flow of new drugs to your patients: The cost of the research is more than ten times what it was, per product, in 1962; and whereas governmental clearance of new drug applications took six months then, it commonly consumes two years now.

The FDA needs adequate time, of course, to consider data. But it is equally clear that the present approval process contributes to needless delay of needed therapy. That's why the increased efficiency of the drug approval process is vital to all our futures.

If these issues concern you, we suggest that you make your voice heard—among your colleagues and your representatives in State legislatures and in Washington.

It could make a difference in your practice tomorrow.

P·M·A

Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W., Washington, D.C. 20005

(Continued from page 817)

THE FARIBAULT CLINIC LTD., has an immediate opening for a General Surgeon who is Board certified or eligible. The Clinic is in a rural community near the metropolitan area and consists of six Family Physicians, one Surgeon and two Internists. For information please write to: Mrs. Arlene Pfeffer, Faribault Clinic Ltd., 924 N.E. 1st St., Faribault, Minnesota 55021.

LE MARS, IOWA, NEEDS THREE FAMILY PHYSICIANS now to provide medical service to a county-seat community of 8,500 and a medical area of 25,000. Three doctors now practicing need immediate help because of the retirement of colleagues. You have your choice of joining existing clinics or establishing your own practice, fully supported by present physicians. New 44-bed municipal hospital entirely paid for by local funds will open this spring. Excellent public and parochial school systems, 4-year accredited liberal arts college, rich agricultural area, variety of diversified clean industries, modern progressive business district and excellent recreational facilities are available for your enjoyment and relaxation. Le Mars is centrally located in northwestern Iowa within easy driving distance to the metropolitan areas of Sioux City, Omaha, Des Moines, Minneapolis and Sioux Falls. If you are looking for quality of life in a wholesome environment, we think you will be interested in Le Mars. For further information contact: Floyd Valley Medical Manpower, 115 Plymouth St. NW, Le Mars, Iowa 51301, phone 712-546-5306.

AVAILABLE—FAMILY PHYSICIAN, married and certified. All interesting situations will be considered—group, partnership or solo. All details of replies will be kept strictly confidential. Write: Minnesota Medicine-5121, 101 E. 5th St., St. Paul, MN 55101.

TWO FAMILY PHYSICIANS with large hospital practice wish third associate who is Board Eligible, to join busy family practice. Located in Waterloo, Iowa, a northeast Iowa community of 75,000. All records dictated on the Problem Orientated Medical Records Systems. Ronald R. Roth, M.D. & Ronald D. Flory, M.D., 611 Black's Bldg., Waterloo, Iowa 50703.

GENERAL PRACTITIONER to join MD in new Clinic in community of 2200; 25 miles southwest of Minneapolis; excellent schools and churches; productive farming area; 10-minute drive to hospital. Declared area of need with grant forgiveness benefits. Write or call Paul A. Stahler, M.D., Amo Vitae Clinic, 310 Sunset Drive, Jordan, Mn. 55352. 612-492-6323.

FAMILY PHYSICIANS needed to join one general practitioner in new medical clinic adjacent to the 35 bed JCAH Hospital in a progressive beautiful lakeside community of 4,000 people. Excellent opportunity for anyone interested in fishing, skiing, golf and lakeside living. For complete details write or call G. E. Lee, M.D. 612-634-4535 (Clinic) or 612-634-4312 (Home).

DERMATOLOGIST wanted to join 17 doctor multispecialty group in southern Minnesota, in the scenic Hiawatha Valley. Salary and fringe benefits competitive. Diversified recreation. Excellent school system including three four-year colleges. For additional information, please write or call Dr. A. E. Edin, Chairman Recruiting Committee, Winona Clinic, Ltd., 420 E. Sarnia St., Winona, MN 55987. (507) 454-3680.

MMI ANNOUNCES STATE-WIDE REGISTRATION. We are presently registering physicians who: (1) Desire coverage for their practice on weekends, or periods of one week to several or more months—OR—(2) Are available to do Locum Tenen on weekends, or periods of one week to several or more months. Write or call M. A. Cornwall, M.D., Medical Director, Midwest Medical, Inc., Lakeland, Minn. 55043—Phone (612) 436-5161.

WANTED—Obstetrician-Gynecologist. 17-man multispecialist group, located in the beautiful Hiawatha Valley, 50 miles south of Minneapolis and St. Paul, seeks Board Certified or eligible OB-GYN to join present two man department. Full sharing in delivery and major surgery at once. No pregnancy terminations. Send curriculum vitae and brief background sketch, experience, family data, etc. Contact: Interstate Medical Center, P.A., Highway 61, West, Red Wing, MN 55066.

FAMILY PRACTITIONER—To join active, two-doctor incorporated group practice in scenic Grantsburg, Wis. Salary open and negotiable. Modern clinic adjacent to 84-bed, JCAH Hospital. Excellent opportunity for M.D. outdoor enthusiast. Fishing, hunting, skiing, snowmobiling, golfing, and lakeshore living nearby. Cultural advantages of Twin Cities 75 freeway minutes away. Three of four weekends off plus one day off per week. Office affiliated with University of Wisconsin preceptorship program. Area qualifies for student loan forgiveness. Please contact: Richard L. Hartzell, M.D., Grantsburg Clinic, Ltd., Grantsburg, Wisconsin 54840. Tel. 715-463-5317.

TAX DEDUCTIBLE VACATIONS FOR MEDICAL PROFESSIONALS. Over 500 listings of national/international meetings in the medical sciences for 1977. Send a $10 check or money order payable to Professional Calendars, P.O. Box 40083, Washington, D.C. 20016.

OB-GYN, PEDIATRICS SPECIALIST needed by 16-man multi-specialty clinic in university community of 50,000 in western Wisconsin; excellent retirement and fringe benefits; fine recreational opportunities; salary negotiable. Send curriculum vitae and references to: John R. Ujda, M.D., La Crosse Clinic, 212 South 11th Street, La Crosse, Wisconsin 54601.

Classified Advertisements

EDINA—Opportunity for a family physician to join an established corporate group of seven physicians. Group currently consists of six family physicians and one general surgeon. Clinic is located approximately one quarter mile from a 450 bed hospital. Contact J. Turonie, Administrator at 612-920-5966.

INTERNIST to join progressive five-man group. Central Minnesota. 130 bed hospital. Lake area. Starting salary $40,000 per year. Fantastic practice opportunity. Contact Little Falls Clinic, Little Falls, Minnesota. 612-632-5305.

CARDIOLOGY and NEUROLOGY specialty positions available with Mankato Clinic, Ltd. This multi-specialty group attracts specialty referrals from a Southern Minnesota Area of 250,000 population. Excellent group practice opportunity in medium sized community with full hospital services; full range of group fringe benefits; liberal time off; salary first year, incentive pay thereafter. For more information call collect 507-625-1811; Byron C. McGregor, M.D., or D. R. Molesworth, Administrator, Mankato Clinic, Ltd., Mankato, Mn. 56001.

NEEDED—INTERNIST OR FAMILY PRACTITIONER to assume a practice in a pleasant lakeside suburb of St. Paul. Write: MINNESOTA MEDICINE-518, 101 E. 5th St., St. Paul, MN 55101.

DOCTORS—THE NEXT MOVE IS YOURS—Midwest Medical, Inc. will provide you with more information about each opportunity than you have ever imagined possible. For the first time you can visually preview the Community and Medical Facilities of over 80 opportunities in the Upper Midwest, at ONE location. Saves you time, expense, and frustration. For a thorough appraisal of all factors involved, please accept our invitation to call. For discreet and confidential assistance contact M. A. Cornwall, M.D., MMI's Medical Director, or write: Midwest Medical, Inc., Lakeland, Minnesota 55043, 612-436-5161. Locum Tenens opportunities always available.

MD AVAILABLE FOR LOCUM TENENS IM or ER, board eligible (Mayo), full time April, May and June 1977. Married. Minimum $1,000/wk, prefer near Rochester but anywhere. CV request, RRI Dodge Center 55927. (374-2453).

INTERNIST—Excellent opportunity for active practice of general internal medicine. Four-man group in North Iowa. Midway between Des Moines and Mpls. Close to Lake. Excellent art museum and school system. Starting salary $40,000, plus bonus. Modern hospital. 35,000 community with 100,000 drawing area. Phone collect at 515-423-0244.

ST. CROIX HEALTH CENTER—New Richmond, Wisconsin. *Psychiatrist-Clinical Director*—Full-time position in a comprehensive center operating in-patient and out-patient mental health programs, in-patient and out-patient alcoholism treatment programs, and programs for the developmentally disabled, including adult day care and sheltered work. Salary is negotiable depending upon background and experience. The facility is situated in a town of 4,000 population 35 miles from downtown St. Paul, Minnesota. Contact—Sumner Bright, Program Director, St. Croix Health Center, Box 99, New Richmond, Wisconsin 54017. Phone (715) 246-6186.

PSYCHIATRIC RESIDENCY—Vacancies for positions for July 1, 1977 for those who have a regular Iowa License or can obtain one by reciprocity or via FLEX. Prepare for career in private practice, community clinics or hospital based psychiatry. Emphasis on close supervision of intensive individual and group psychotherapy, OPD, Children's Unit, Adolescent Unit. Neurology affiliation with University of Iowa. The stipends are: 1st yr $21,294; 2nd yr $22,360; 3rd yr $23,478. Intensity and diversity of training program appreciated best by personal visit. T. B. McManus, M.D., Superintendent, Mental Health Institute, Cherokee, Iowa 51012. Equal Opportunity Employer, Call Collect 712-225-2594.

OBSTETRICIAN to associate with Ob-Gyn Department of established multispecialty group in St. Paul-Minneapolis and suburban areas. Excellent salary, generous fringe benefits. Tremendous growth potential in one of America's leading metropolitan areas. Curriculum vitae and references invited. Box 80100, St. Paul, Minnesota 55108.

NEEDED—Family Practice opportunity in Rich farming community, West Central Iowa. Beautiful, progressive city with new 100 bed hospital. Five minutes to hospital. Friendly community, good production contract, well established six man group, short time to full partnership. Call Ed Murphy, Carroll Medical Center, 502 N Court, Carroll, Iowa 51401, 712-792-1500.

SEEKING INVESTMENT partner for Caribbean scuba diving venture. Business has track record and is currently active. Operates under U.S. tax laws. $25,000 range desired for expansion. For more information, write: MINNESOTA MEDICINE, 101 E. 5th St., St. Paul 55101.

OPHTHALMOLOGIST—Established multispecialty group in St. Paul-Minneapolis area seeks additional ophthalmologist. Excellent earnings, above average benefits. One of America's leading metropolitan areas. Excellent schools, variety of cultural and sporting events. Curriculum vitae, references invited. Box 80100, St. Paul, Minnesota 55108.

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Index to Advertisers

Allied Medical Audit Control, Inc. 822
Anderson, C. F., Co. 794
Beltone Electronics Corp. 811
Burroughs-Wellcome Co. 802
Classified Advertising 817
Kjell Bergh's Borton Leasing, Inc 744
Hearing Instrument Dispensers Guild, Inc. 738
Lilly, Eli, & Co. 746
Medical Protective Company 744
Minnesota Medical Seminars 804
Pharmaceutical Mfrs. Assn. 818, 819
Roche Laboratories .... Cover 2, 735, 794, 795, Covers 3-4
Roerig and Company 796
Smith, Kline & French 813
U.S. Navy Recruiting District 736
Upjohn Company 814, 815, 816
Volvo, Kjell Bergh's Borton 744

Ernst Simonson Memorial Lectureship

The first Ernst Simonson Memorial Lectureship was delivered by Dr. Eliot Corday of Los Angeles, California, September 21, 1976 at Mount Sinai Hospital, Minneapolis, Minnesota. This lectureship was established by the late Ernst Simonson, distinguished electrophysiologist, to be given annually, alternately at Mount Sinai Hospital in Minneapolis and at the Annual Meeting of the American Heart Association Minnesota Affiliate.

minnesota medicine

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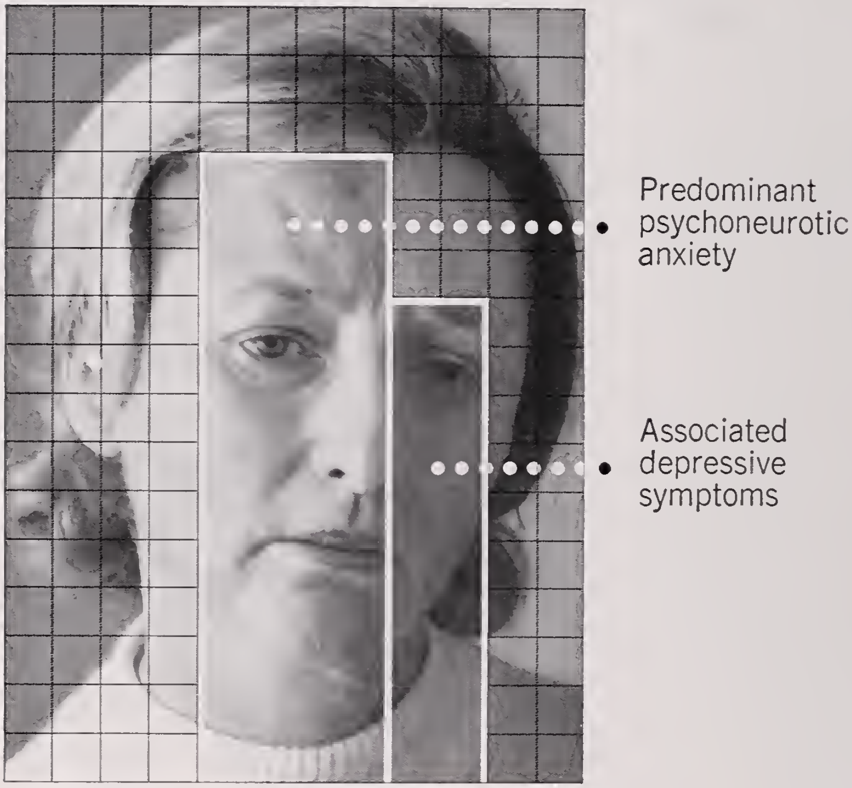
Predominant psychoneurotic anxiety
Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency
and/or severity of grand mal seizures
require increased dosage of standard
convulsant medication; abrupt withdr
may be associated with temporary in-
crease in frequency and/or severity o
seizures. Advise against simultaneous
gestion of alcohol and other CNS depr
sants. Withdrawal symptoms (similar
those with barbiturates and alcohol) h
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anxiety states
with associated
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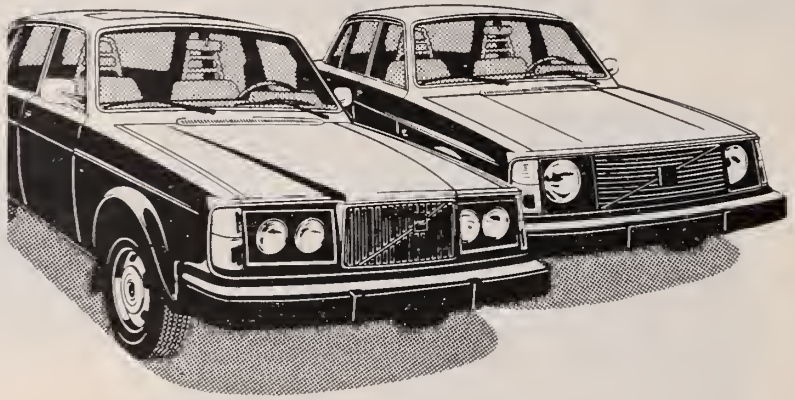

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President's Letter

Can I Stay in Medical School?

Would you believe increasing numbers of students in Minnesota's three medical schools are finding it difficult to continue their medical education for financial reasons? For some students lack of money may interrupt or postpone their educational objectives. The situation is serious. The need for physicians to assist the young men and women who are preparing to represent the medical profession in the future is near. Severe cutbacks in traditional sources of funding have occurred (i.e. the Federal Health Professional Loan and Scholarship program is being phased out). Students have been placed on a year around —four quarter—school year so part-time employment to supplement their income is impossible. Recently over the strong opposition of the MSMA, medical school tuition was doubled.

Now a new problem has arisen—to use the vernacular —our own well has gone dry. Of all the MSMA functions, the Medical School Loan Fund program has an outstanding record of success. Within a span of 15 years, 212 interest free loans amounting to $154,765 have been made to help needy students in Minnesota's three medical schools. Even more remarkable is the fact that in all this time there has not been a single default but now we are without funds and have thirty loan applications before us.

To qualify, students must have satisfactorily completed one quarter of medical school and be currently enrolled in a program leading to the degree of Doctor of Medicine. Loans are limited to $900.00 for a student during any one year. The loans are interest free until graduation, earn 8% per annum thereafter, and are due and payable within three years of graduation. If the student terminates his studies prior to graduation, the loan becomes immediately due and payable. Loan recipients must be members of the appropriate county medical society and the MSMA. Currently medical students are required to pay a one time dues of $10.00 ($5.00 county, $5.00 state). Medical school membership carries with it all the rights and responsibilities of regular membership except the right to hold office.

To solve this problem a special fund-raising committee under the chairmanship of Dr. John Regan is making a concerted effort to obtain a tax exempt contribution from all Minnesota physicians. Approximately $70,000 is needed immediately to meet anticipated student needs through the 1976-77 school year. To meet future needs and make the fund self-sufficient, a long term goal of $400,000 has been established.

Our first request for a generous gift was mailed in September, a second request will be mailed in December and concomitantly efforts will be directed toward periodic contributions, bequests, memorials and special gifts from foundations, Minnesota based companies and non-Minnesota firms who do a substantial medical supply business in Minnesota.

Make your tax exempt contribution now—don't force our future physicians to either join the National Health Service Corps for subsistence or to emulate from wealth.

Richard E. Anonsen, M.D.
President
Minnesota State Medical Association

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Editor's Notebook

what the dickens
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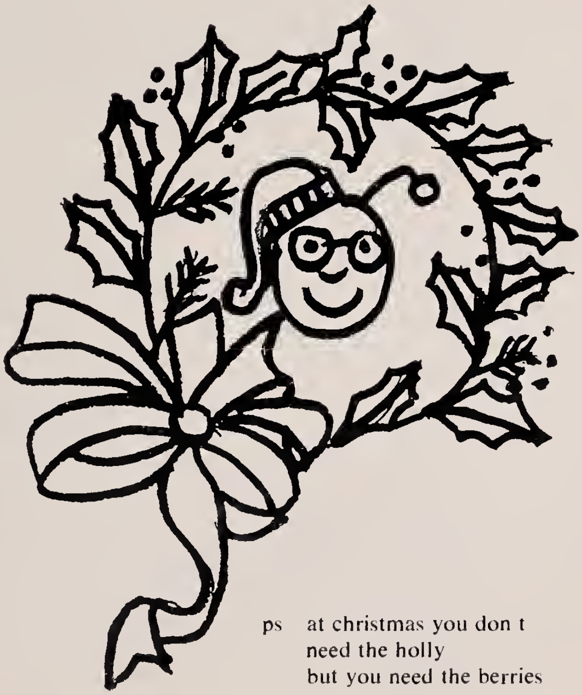
has delegated me
the duty of
wishing you
a merry christmas
in an original way
what the dickens
does he mean
and how in the dickens
do you do it
how can you
be creative
about christmas
you can t be cynical
and you can t make fun
or even pun
and even though
i am a literary
cockroach i have
enough class not
to bug you about christmas
so maybe the best thing
is to quote the great man
himself who said

"i do come home at christmas
we all do or we all should
we all come home
or ought to come home
for a short holiday
to take
and give a rest"
charles dickens

what the dickens
was i worried about
it is plain and simple
go home on christmas
take a rest and
give your family one
why in the dickens
didn t i think of that
minny



ps at christmas you don t
need the holly
but you need the berries

Student Loan Fund

In 1958 your State Medical Association through its Council recognized that many needs of its members and future members were going unmet. The response was the establishment of a charitable foundation. Incorporated in 1959 the articles state: "The corporation is organized and shall be operated exclusively for the benefit of, to perform functions of, and to carry out the religious, charitable, literary, and educational purposes of the Association."

In the intervening years the Foundation has done just that. One of its principal activities has been the Physician's Assistance Program to provide supplementary support to those doctors and their widows who are in need. Funded by a $4.00 increment of your annual dues, this effort has provided more than $200,000 of aid to physicians or physician's widows who have come on bad times. The late beloved James Blake guided that segment of the Foundation for years. Those of you who knew him, well remember the ferocity with which he guarded that activity as well as the love he lavished on those recipients of our beneficence.

The Rural Family Practice Scholarship Program is another Foundation Activity. Now disbanded, it aided twenty-seven students during its years of activity.

More recently the Foundation has concentrated on providing long term loans to Medical Students. These loans are interest-free until graduation, after which they gather interest at 8% per annum. So, the fund is revolving and even gains slightly as a result of its interest feature. In its long and honorable history it has not lost a single loan by default.

New times make new needs. Traditional sources of student aid have evaporated, and more of these young people are turning to their seniors for aid. The advantages are obvious. The loan fund helps those who will one day replace us. Additionally, the loan procedure introduces these men and women to the ranks of organized medicine early in their careers.

The pressure for loans has depleted Foundation resources. We are all loaned out! At this moment there are 30 applicants. There will be more after the fall quarter. Seventy thousand dollars is necessary to meet present needs. Here is an opportunity in the final month of your fiscal year to make a fully tax deductible charitable contribution to a cause as good as you will ever find. So, while the mood is on you . . . send your generous check to the Minnesota State Medical Association Foundation Student Loan Fund, 101 East Fifth St., St Paul, MN 55101.

John J. Regan, M.D.
Chairman

Cover Photograph

"Cupping Therapy—Fort Snelling Hospital 1825"

Mr. Christopher Born is a student of photography at the College of Arts and Design, Minneapolis, and took the cover photo to accompany David Wiggins' paper "First Minnesota Hospital" on page 867 of this issue.

This is the hospital ward room in the restored hospital at the Fort Snelling Restoration and is restored back to the period of 1825.

Contents—December, 1976

Volume 59-12
Pages 823-890

COVER PHOTO—"Cupping Therapy—Fort Snelling Hospital 1825"
Christopher Born 830

PRESIDENT'S LETTER—Can I Stay in Medical School?
Richard E. Anonsen, M.D., President 827

EDITOR'S NOTEBOOK—what the dickens
minny 829

ORIGINAL CONTRIBUTIONS

Mobile Coronary Care in the Management of Prehospital Cardiac Arrest
Frederic J. Engman, M.D. et al. 833

Simple Osteotomy for Hallux Valgus
Michael Davis, M.D. and Thomas Litman, M.D. 836

Effect of Placebo on Exercise Response and Nitroglycerin Consumption
Keith E. Hartman, M.D. et al. 839

Chemodectoma with Multiple Skeletal Metastasis and Anemia
Robert A. Sweet, M.D. et al. 844

EDITORIALS

Semen Analysis and Male Fertility
William L. Engel, M.D. 853

Unstable Diabetes
William J. Bergstrom, M.D. 853

Transcutaneous Stimulation for Chronic Pain Relief
Richard F. Galbraith, M.D. 855

Acute Diabetic Complications
Rudolph Ripple, M.D. 855

Chemodectoma
J. Michael Ryan, M.D. 857

Education of the Diabetic Patient
Lois Recker 857

HISTORY—Minnesota's First Hospital
David S. Wiggins 867

REVIEW—Semen Analysis and Male Fertility
Zoltan Posalaky, M.D. 877

MSMA HIGHLIGHTS—Looking Ahead—the 1977 Minnesota Legislature
C. A. Anderson, M.D., Chairman
MSMA Committee on Legislation 859

HAIR TODAY: GONE TOMORROW
John T. Pewters, M.D. 887

CONTINUING MEDICAL EDUCATION 848, 887, Index 6

CLASSIFIED ADVERTISEMENTS 862

INDEX TO ADVERTISERS 890

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Mobile Coronary Care in the Management of Prehospital Cardiac Arrest

St. Paul, Minnesota Experience

FREDERIC J. ENGMAN, M.D.;* BRIAN C. CAMPION, M.D.;*
JOHN W. McBRIDE, M.D.;* PRADUB SUKHUM, M.D.;* and LINDA A. LONG, M.D.*

The first full year's operation of the St. Paul expanded emergency system which includes mobile coronary care is described. One-hundred ninety-nine patients with out-of-hospital cardiac arrest were seen with data available on 186 patients. Sixty-four of those patients or 34.4% survived to reach the hospital after treatment by paramedical personnel in voice and telemetry contact with physicians at St. Paul-Ramsey Hospital and Medical Center. Twenty-three patients or 12.4% survived to leave the hospital. Of patients presenting with tachydysrhythmias, 16.9% survived while only 1.9% presenting with bradydysrhythmias lived. We believe that mobile coronary care units, in conjunction with public education as to early warning signs and widespread training in cardiopulmonary resuscitation are of value.

OVER 50% OF ALL deaths from ischemic heart disease occur outside of the hospital, often suddenly and without warning.[1] In an attempt to reduce this large mortality, expanded emergency systems including mobile coronary care units have been established in many cities throughout the world.[2-7] Many of these programs utilize highly trained emergency medical technicians often called paramedics. We are reporting the St. Paul Fire Department Paramedic system's experience in the treatment of out-of-hospital cardiac arrest during 1974, their first full year of operation.

Methods

The St. Paul Fire Department Paramedic system began operation in September 1973 with two units. In 1974 there were four paramedic units and four other fire department ambulances responding to approximately 10,000 calls. Details of program implementation and the educational program are published elsewhere.[8] In 1974, 38 paramedics had been trained as described.

Any citizen within the city limits of St. Paul may activate the system by calling the fire department's emergency number. The ambulance nearest the patient site will respond with an average response time of slightly under four minutes. In cases thought to be cardiac, severe trauma, or other critical illness, the nearest paramedic unit is also dispatched.

At the patient site the paramedics perform goal-directed history and physical examinations and transmit this information to a physician either in the coronary care unit or the emergency room at St. Paul-Ramsey Hospital, depending on the nature of the call. A single lead monitor strip may be transmitted. When cardiac patients are stabilized using appropriate drugs, defibrillation, and ventilation adjuncts, including oral and esophageal airways, they are transported to the area hospital of their choice. We have direct admitting privileges to all St. Paul hospital coronary care units with one exception.

Data Gathering

The paramedics participated in approximately 10,000 calls in 1974. Of these 10,000 calls, 199 cases of cardiac arrest were seen and therapy instituted. Cardiac arrest was defined as the ab-

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*Section of Cardiology and Department of Medicine, St. Paul-Ramsey Hospital and Medical Center and the University of Minnesota.

The study supported in part by a grant from the Minnesota Heart Association.
Reprints from Brian C. Campion, M.D.

sence of spontaneous respiration and the inability to obtain pulse or blood pressure. Information on these victims was obtained by reviewing the hospital records and the emergency room log books at the hospitals to which they were transported.

The presenting rhythm disturbances were also reviewed. We divided them into tachydysrhythmias and bradydysrhythmias, the former consisting primarily of ventricular fibrillation and ventricular tachycardia with five cases of supraventricular tachycardia. The bradycardias included idioventricular rhythms, asystole, complete heart block and sinus bradycardia. This information was obtained by reviewing the 15-20 second rhythm strip recorded on the paramedics initial contact with the patient. In eight instances rhythm strips were not available due to technical difficulties: these were not included. The diagnosis of an acute myocardial infarction was made by the appearance of new Q waves by electrocardiogram.

A review of patient survival in cardiac arrest prior to the paramedic program was obtained by examining emergency room log books and hospital records data on the cardiac arrests which were transported to or occurred in the St. Paul-Ramsey Hospital Emergency Room during a 12 month period between January 1972 and July 1973.

Results

Table 1 shows that of the 199 patients with the diagnosis of cardiac arrest, we were able to obtain information on 186 or 94%. Ages ranged from 10-94 years with a mean age of 63.5 years. Men outnumbered women by slightly greater than a 2:1 ratio. Information as to the sex of the patient was not recorded in 31 instances.

TABLE I
Prehospital Cardiac Arrest
(St. Paul, Minnesota Experience
January 1974—December 1974)

Total number of patients	199
Number with information on survival	186
Mean age	63.5 years
Age range	10-94
Male	117
Female	51
Unknown	31

Table 2 shows that approximately two-thirds of our 186 patients were pronounced dead on arrival at the hospital. Of the remaining patients, 41 patients died in the hospital and 23 or 12.4% survived to leave the hospital. The majority of the hospitalized non-survivors died a brain death. To our knowledge, none of the survivors was discharged with severe neurological dysfunction. A diagnosis of an acute myocardial infarction was made in six of the survivors or 26%.

TABLE 2
Prehospital Cardiac Arrest

	Number	%
Patients with information on survival	186	
Dead on arrival at hospital	122	65.6
Survived to reach hospital	64	34.4
Died in hospital 1-40 days	41	22
Survived to leave hospital	23	12.4

In review of 111 cardiac arrests which were managed in the St. Paul-Ramsey Hospital Emergency Room prior to paramedic mobile coronary care units, we found that five or 4.5% survived to leave the hospital.

Tachydysrhythmias were present in two-thirds of the arrests and carried the most favorable prognosis (Table 3). Twenty-one out of the twenty-three survivors had an initial tachydysrhythmia. There were 54 patients with bradydysrhythmias, making up 29% of our population. Of the patients with tachydysrhythmias, 16.9% survived to leave the hospital whereas only 1.9% of the bradydysrhythmias survived. Three of five patients with supraventricular tachycardia survived. Survival for those presenting with ventricular tachycardia or fibrillation was 15 of 119 or 15%.

TABLE 3
Initial Rhythm Disturbance—Prognostic Implications

Presenting Rhythm	Number	%	Number Surviving	% Surviving
Tachydysrhythmias	124	66.7	21	16.9
Bradydysrhythmias	54	29.0	1	1.9
Indeterminate	8	4.3	1	12.5

Discussion

Pantridge[9] and, more recently, Crampton[5] and Liberthson[6] have shown the value of mobile coronary care units in the management of prehospital cardiac arrest. Our figure of 15% success rate in cardiac arrest victims in which the initial rhythm disturbance was ventricular tachycardia or fibrillation is comparable to that obtained in these studies.

TABLE 4
Conventional Management Cardiac Arrest

St. Paul-Ramsey Emergency Room February 1972—July 1973	
111 Cardiac arrests	4.5% Survived to leave hospital

We attempted to evaluate our overall 12.4% survival with that of those transported by lay personnel or untrained ambulance attendants to a county hospital emergency room. The 4.5% survival rate is not a comparable figure because information on whether these patients received cardiopulmonary resuscitation (CPR) prior to hospitalization was not available. Also, some of the arrests occurred while the patient was in the emergency room. We feel that this two to threefold difference in survival is of interest and may be even greater if identical patient populations were studied.

Analysis of the presenting rhythm disturbances in cardiac arrests identified the tachydysrhythmias, primarily ventricular fibrillation, as being the most common (66.7%) and associated with the best prognosis (16.9%) for survival to leave the hospital. This is in agreement with studies done by Liberthson.[10]

It has become increasingly evident that survival in cardiac arrest is directly related to initiation of basic life support. While our response time of slightly less than four minutes is within an acceptable limit, the major delay remains the patient delay prior to summoning assistance. Approximately 40% of deaths from acute coronary disease, occur in less than one hour after onset of symptoms.[11] Therefore successful public education is essential if survival from out-of-hospital cardiac arrest is to improve.

One approach to reducing mortality is that of Cobb and associates in Seattle.[12] Coincidental with training 80,000 people in basic life support, survival from out-of-hospital cardiac arrest increased from 13% to 25%. At present one in five cardiac arrest victims have CPR started by non-emergency personnel.

The mobile coronary care unit performs functions other than therapy for cardiac arrest. Acute cardiac victims may have premonitory dysrhythmias treated thereby preventing fatal rhythm disturbances. The effect of pain relief in decreasing infarct size has not been evaluated but could theoretically be a significant factor. Crampton has estimated that the addition of a mobile coronary care unit to a hospital coronary care unit has saved 15.2 lives per 100,000 population annually.[5]

Our results of 12.4% overall survival in patients with out-of-hospital cardiac arrest and 16.9% in patients presenting with tachydysrhythmias are encouraging since they compare with similar systems operational for longer periods of time. It is obvious, however, that mobile coronary care alone will not dramatically improve survival from sudden cardiac death but must be combined with programs in public education and cardiopulmonary resuscitation. We believe that the addition of mobile coronary care to a community's emergency system will result in the saving of a larger number of lives and is, therefore, a worthwhile program.

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Shotwell Award

O. L. N. Nelson, M.D. is the 1976 recipient of the Shotwell Award for noteworthy efforts in the field of health care. The award is presented annually by the Metropolitan Medical Center, Minneapolis. In 1974 he was given the distinguished Service Award by the Minnesota State Medical Association—their highest award for outstanding service to the organization and to the practice of medicine.

Simple Osteotomy for Hallux Valgus

MICHAEL DAVIS, M.D.* and THOMAS LITMAN, M.D.*

A simple oblique osteotomy for bunion is described. It can be rapidly performed and does not violate the metatarsophalangeal joint. The procedure is applicable to both young and old, has been associated with few problems, and is satisfactory both for pain relief and cosmetic improvement.

Most would agree that surgery for hallux valgus is indicated primarily to relieve pain and seldom for cosmetic reasons alone.[2] An operation that will routinely produce a more comfortable foot, and one which looks better as well, is an added bonus to the patient. Many procedures have been devised with this in mind including soft tissue operations,[4,9] hemiarthroplasty,[5,8] arthrodesis,[10] and osteotomy of the proximal phalanx of the great toe.[1] They have been associated with varying degrees of success.

Some form of first metatarsal osteotomy would seem to have the greatest chance of producing a comfortable good-looking foot. This corrects the metatarsus primus varus and allows relaxation of the lateral capsular structures and adductor hallucis tendon. Both help to prevent recurrence. With displacement of the osteotomy, the articular relationship between surfaces of the first metatarsophalangeal joint is changed, assisting in relief of pain. Operations to correct a bunion by osteotomy of the first metatarsal have been described by a number of authors.[3,6,7,11,12] Many of these procedures are technically complex, require careful shaping of osteotomized surfaces, removal of bone wedges, and often fixation of the osteotomy using suture threaded through bone only with great difficulty.

J. N. Wilson[12] described an oblique osteotomy of the first metatarsal neck, combined with removal of the exostosis. The latter required opening of the first metatarsophalangeal joint. It was a relatively simple and rapidly performed operation and one associated with a high degree of success. He advocated the procedure primarily for adolescents and young adults.

B. J. Dooley[3] used Wilson's technique with one exception: the medial exostosis was not removed. This allowed the first metatarsophalangeal joint to remain undisturbed. He felt that the less interference with this joint, the better. Dooley's paper was presented at the combined meeting of the Australian and New Zealand Orthopedic Associations in Adelaide. As far as we can determine it only appears in brief form in the Proceedings of the JOURNAL OF BONE AND JOINT SURGERY, August, 1968. Because it is a simple procedure, rapidly done, associated with few problems and almost uniform success, we believe it warrants greater exposure. Our interpretation of his procedure follows.

The Operation

Either spinal or general anesthesia is used. A tourniquet is applied to the upper thigh and inflated to 500 mm. Hg. A longitundinal dorsal incision is made over the distal first metatarsal. The extensor mechanism is retracted and the distal metatarsal shaft and neck are exposed subperiosteally. Care is taken not to violate the metatarsophalangeal joint. Small Chandler retractors placed around the bone facilitate exposure and protect soft tissue structures. Using a small hand drill multiple holes are made to outline an approximately 30° osteotomy site (Figure 1). Splintering of the bone has not been a problem when this is done. The osteotomy is now completed using a thin bladed hoke osteotome. The 30° surface cut exposes a broad expanse of bone for healing. A power saw is not used since the authors feel that cold steel is gentler on a cellular level than a hot rapidly oscillating blade, making non-union less likely. The distal fragment is allowed to slip proximally and laterally, relaxing the lateral capsule and adductor hallucis (Figure 2). A small bone rongeur is used to trim the sharp medial bone fragment (Figure 3). Nothing is done to the lateral fragment. Internal fixation is not used. After lavage with normal saline the deep fascia is approximated using a few interrupted sutures of plain catgut and the skin is closed using intracuticular wire. While the great toe is held in about 5° of varus a footlet (or great toe spica) cast is applied. With the toe in slight varus, approximation of the osteotomized fragments is assured, no internal fixation is necessary and union is rapid.

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Postoperative Care

Usually the patient is discharged from the hospital on the third or fourth postoperative day. Weight bearing on the heel is encouraged as soon as the patient can tolerate it. Often the patient will begin to bear some weight on the forefoot as well. This is not discouraged, since it tends to promote healing of the distal fragment in optimum weight bearing position. At two weeks the cast is changed, sutures are removed, an Xray is taken and a second footlet cast is applied with the great toe in neutral position. Usually the osteotomy is clinically and radiographically solid at six to eight weeks and all immobilization can be discarded.

An illustrative case is presented in Figures 4-6.

Conclusions

We have used this procedure to the exclusion of all others since 1969. We have used it on teenagers and senior citizens alike with no modification. Absence of classical metatarsus primus varus does not seem to preclude a good result. Likewise the presence or absence of osteoarthritic

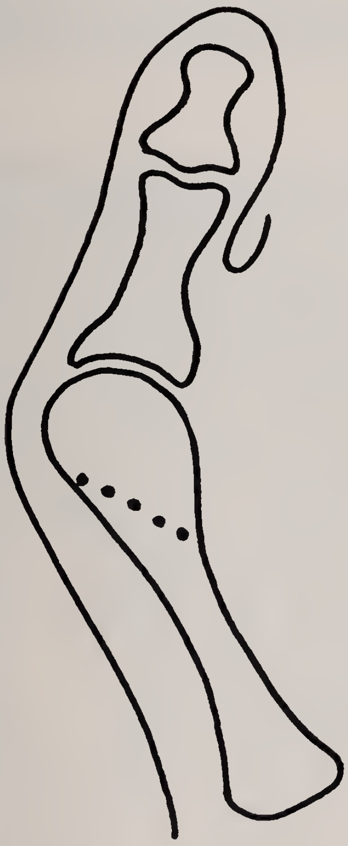

Fig. 1—The osteotomy is outlined using small drill holes.

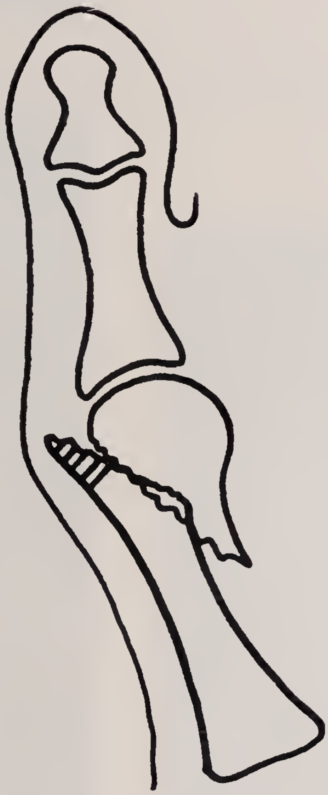

Fig. 2—The osteotomy is completed and allowed to displace.

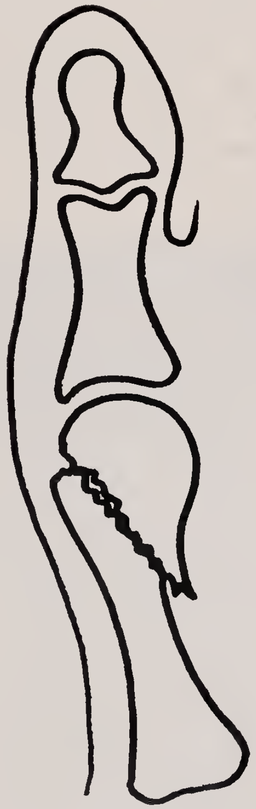

Fig. 3—The medial bone spike is removed using a small rongeur.

change in the metatarsophalangeal joint has not appreciably affected the outcome. Infection has not occurred, probably due to the rapidity of the procedure and the minimal exposure of soft tissues. No non-unions have resulted. One delayed union in a forty year old woman occurred but prolonged immobilization in plaster for sixteen weeks eventually resulted in consolidation of the osteotomy. The patients have been uniformly pleased with both relief of pain and cosmetic improvement.

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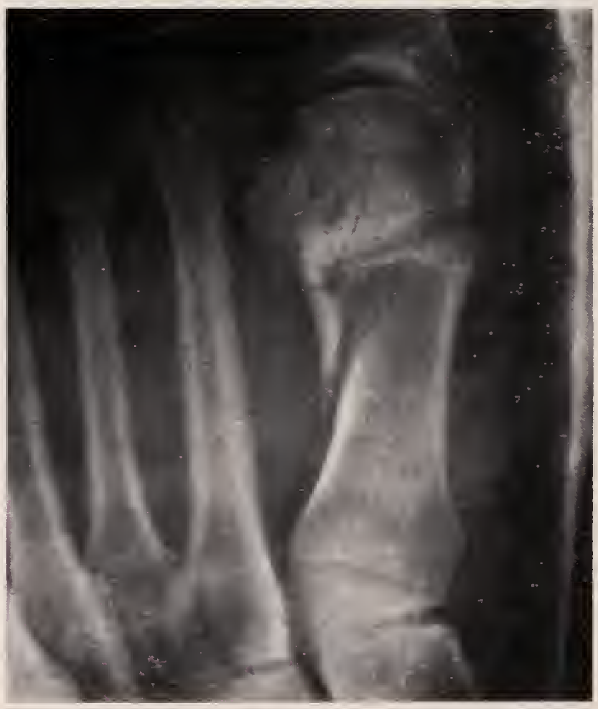

Fig. 5—Immediate postoperative roentgenogram taken through plaster.

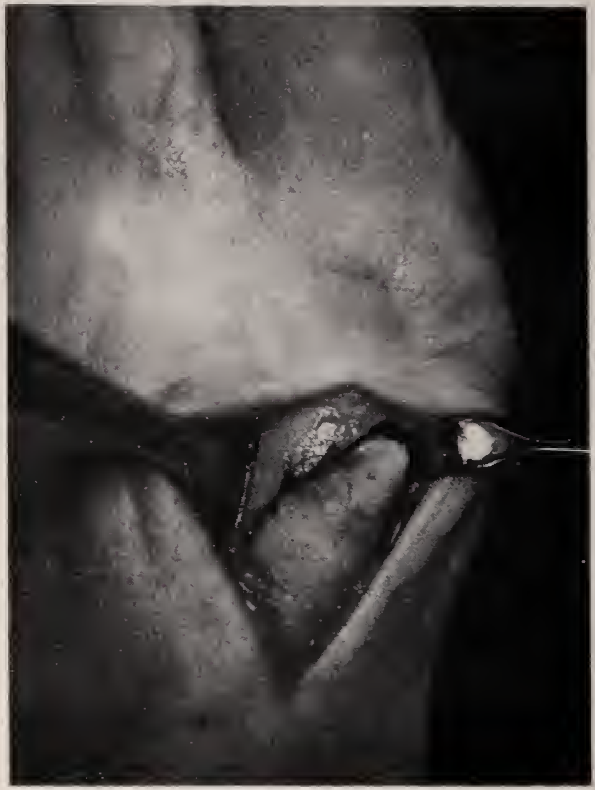

Fig. 4—The osteotomy.

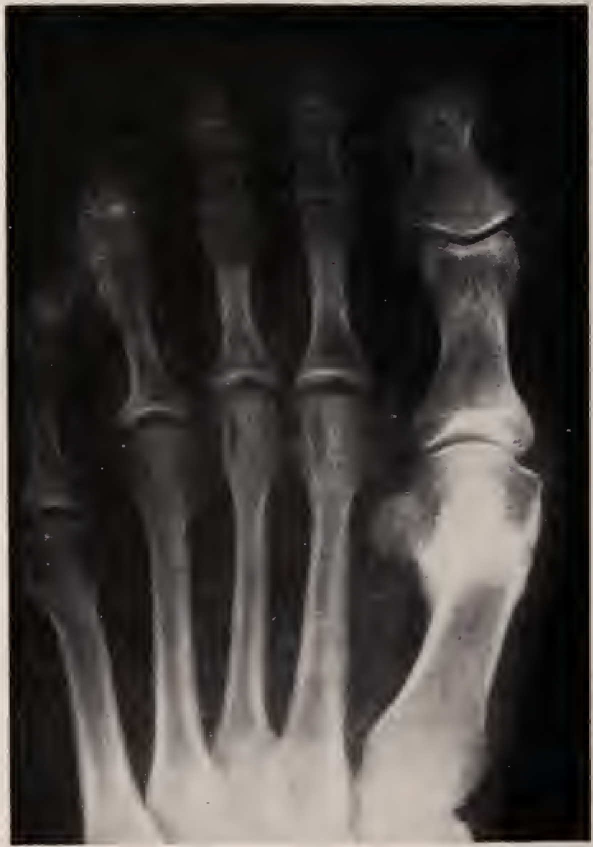

Fig. 6—Roentgenogram taken six months post surgery.

Effect of Placebo on Exercise Response and Nitroglycerin Consumption

KEITH E. HARTMAN, M.D.;* LEONARD A. NORDSTROM, M.D.,* and
FREDARICK L. GOBEL, M.D.*

Nitroglycerin (TNG) consumption and exercise testing are commonly used to evaluate antianginal therapy. It is important therefore to assess their reliability. Twenty patients with either arteriographically proven severe coronary artery disease or documented myocardial infarction were followed with monthly exercise tests while receiving placebo therapy. Diaries indicated that a reduction in the frequency of angina resulted in decreased TNG consumption in 13 of 20 patients (65 percent), while total TNG consumption decreased by 36 percent. Exercise tests demonstrated no significant difference in heart rate (HR), HR x blood pressure (BP) or total exercise time to symptom-limited maximum exercise from month to month. Coefficient of variation (S.D. of mean/mean) was six percent for HR, 10 percent for HR x BP. 19 percent for exercise time and 28 percent for TNG consumption. These data indicate that objective measurements are necessary since placebo effect can severely distort evaluation of antianginal therapy when measured by TNG consumption and frequency of anginal pain. The easily measured physiologic variables of HR, HR x BP, and exercise time were reproducible at symptom-limited maximum exercise over a three month period and were unaffected by placebo therapy.

THE STRONG PLACEBO effect from both medical and surgical treatment of patients with angina pectoris requires objective measurements of functional capacity. Nitroglycerin (TNG) consumption, as an indication of the frequency of anginal attacks is commonly used to evaluate therapeutic response.[1,2] The frequency of angina pectoris in a given patient, however, is regulated by the myocardial oxygen demand which in turn is influenced by a number of factors including the amount and type of exercise performed and the level of anxiety. A change in living habits may result in decreased myocardial oxygen demand, symptomatic improvement, and reduction of TNG consumption with no improvement in exercise tolerance.

Previous studies have indicated that exercise stress testing is a valuable means of assessing functional improvement.[3,4] Variables, commonly measured during exercise to assess functional improvement have included the duration of exercise, external work accomplished, maximum heart rate (HR) achieved, and the product of the maximum HR and components of the blood pressure (BP). During repeated exercise testing patients appear to achieve a similar HR at the onset of angina when there is adherence to a suitable protocol regardless of subjective change.[3,5] The external work accomplished at the onset of angina may, on the other hand, be altered by medical therapy.[6] Most studies of the reproducibility of exercise testing in patients with angina have been conducted over short intervals of time and few variables have been measured.[3,5,7] There is need for additional data to test the long term reproducibility of easy measured hemodynamic variables at the onset of angina during progressive exercise testing.

The purpose of the present study in patients receiving a placebo was two-fold; (1) to test the reproducibility of easily measured hemodynamic variables at the onset of angina during treadmill exercise testing over a period of months; (2) to compare the results of exercise test measurements (objective change), with change in TNG consumption (subjective change).

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Methods

The patient material consisted of 20 men, average age 54 years, with a history of stable angina pectoris of at least one year's duration. The patients were the first 20 members of a larger group to complete the placebo period of a study designed to evaluate a newer antianginal drug. Coronary arteriography in 18 of the 20 patients revealed severe three vessel disease in 14 and severe two vessel disease in two. The remaining two patients had severe disease of the left anterior descending coronary artery, and one of those two patients had a previous anterior wall myocardial infarction. The two patients without coronary angiography had electrocardiographic evidence of a previous myocardial infarction. Many of the patients had been offered surgical therapy. All were chosen on the basis of sufficient motivation to faithfully take medications, complete a TNG consumption diary, and return monthly for testing evaluation.

During testing there was no change in the patients' smoking habits, level of BP, or weight (averaging 177 pounds at entrance into and 178 at the termination of the study). Equal numbers of patients were admitted during summer and winter months. With the exception of four patients, the resting diastolic BP was normal. In these four patients the resting diastolic pressure ranged from 90 mm. Hg to 100 mm. Hg. These four patients were treated with a thiazide diuretic.

The study encompassed a three-month interval during which patients received a placebo medicaton which was taken three times daily. Patients were told that they were entering a drug study which would begin with placebo therapy, but no patient knew how long the placebo period lasted. All patients had performed at least one multistage exercise test before entering the study. Following a control exercise test, patients were retested after one and three months of placebo therapy. Patients were seen at monthly intervals, the diary of TNG consumption was noted, and patient compliance was evaluated by noting the number of pills returned.

Patients exercised upright on a motor-driven treadmill according to a protocol devised by Bruce and Blackmon.[8] A modified Blackburn lead system[9] combined with an inferior lead was used for constant monitoring of the exercise electrocardiogram (EKG) on an oscilloscope, and each minute a permanent recording was made. Prior to, and immediately following exercise a seven lead EKG (limb leads and Blackburn lead) was recorded. The BP was determined from an external cuff and Korotkoff's sounds immediately before exercise, each minute during exercise, and for eight minutes in the post exercise period. In all patients Phase 1 Korotkoff sounds were clearly auscultated throughout the exercise. At the termination of exercise, ST depression was noted and the duration of exercise recorded to the nearest 15 seconds. HR and BP were measured during the final 10 seconds of exercise. Exercise studies were performed only in the morning. Patients were fasting at the time of the exercise test, and were instructed to refrain from smoking for six hours prior to the test.

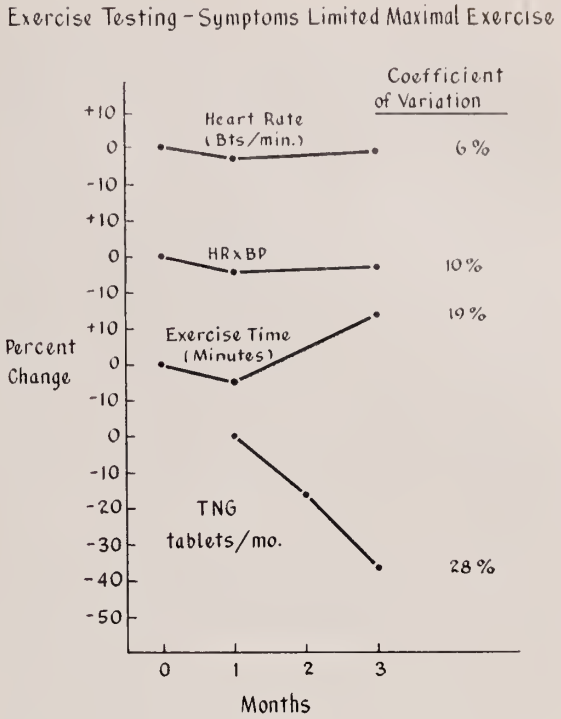
Patients were instructed to grade chest pain in four categories (0 to 4+). One plus chest pain, 25 percent of the most severe pain experienced by the patients, was considered to be mild pain usually not requiring TNG. Two plus pain, 50 percent of the patient's most severe pain, was considered to be of a quantity such that the patient would take TNG. Three plus was 75 percent of his most severe pain while four plus would be the equivalent of the most severe pain that the patient had experienced, comparable in many instances to that of an acute myocardial infarction. Two plus chest pain was used as the endpoint for each exercise test. This grading system has been used with success by others.[10]

Routine medication during the placebo period consisted of TNG, placebo medication, and a diuretic for four patients. No patient received digitalis. To exclude any effects due to nitrate therapy, subjects were instructed to take no TNG for at least an hour before the test.

Standard statistical methods were used in evaluation of these data.[11] Significance was determined by the Duncan multiple range test.[12] The coefficient of variation (standard deviation divided by the mean) was used as a measure of variation for each variable obtained during exercise testing.[11]

Results

Although many patients had a striking reduction in TNG consumption, the group change was not statistically significant. Nine patients reduced TNG consumption by 70 percent and, in 13 of the 20 cases, consumption dropped by at least 25 percent. Six patients showed an increase in TNG consumption; one patient showed no change. The resulting coefficient of variation was 28.3 percent. The reduction in TNG was similar for patients using large numbers of tablets (greater than 100 tablets per month) and for patients using fewer than 100 tablets per month. Mean TNG consumption dropped from 65 tablets during the first month to 55 in the second month to 42 at the end of the study. Despite a 36 percent reduction in TNG consumption from the first month to the third month there were only small changes in mean exercise testing time and maximal mean HR for the three tests (Figure). There was no significant difference in any of these variables for the three tests using Duncan's multiple range test.[12] The coefficient of variation was least for HR and BP at 6 percent (Table), while the value for HR x BP was 10 percent and for duration of exercise was 19 percent (Table). The mean maximal values for HR, BP, HR x BP, and exercise time at the time of two plus chest pain for the first, second, and third tests are given in the Table. There was no correlation between the change in exercise time and the change in TNG consumption. Two patients had ½ mm. ST depression at the onset of exercise. At the termination of the test, all patients but one had at least ½ mm. of ST segment depression at 80 milliseconds from the j-junction. Seventeen patients had greater than 1 mm. of ST segment depression at the termination of exercise, four patients had between 2 and 3 mm. and three patients had over 3 mm. of ST segment depression.



Figure—The percent change from the first test or the first measurement (TNG consumption) is indicated on the ordinate. (HR = heart rate, HR x BP = heart rate times blood pressure product, TNG cons. = nitroglycerin consumption, and C.V. defined in text.)

Discussion

The placebo effect is particularly marked in patients suffering from pain. The efficiency of placebo in the relief of pain has been the subject of several large investigations. Beecher found that severe post-operative pain was relieved by placebo in over 30 percent of patients. In his summary, a compilation of 15 studies of 1082 patients suffering from various types of pain, placebos of-

TABLE

Mean (20 pts)	1st month	2nd month	3rd month	Mean 3 months	Coef. of variation
HR (bts/min)	132	130	132	131	6%
S.D.	± 17	± 15	± 13	± 15	
BP (mm. Hg)	154	150	151	152	6%
S.D.	± 16	± 15	± 15	± 15	
HR x BP	20.3×10^3	19.5×10^3	19.8×10^3	19.9×10^3	10%
S.D.	$\pm 2.9 \times 10^3$	$\pm 1.6 \times 10^3$	$\pm 2.4 \times 10^3$	$\pm 2.3 \times 10^3$	
Time (Min)	4.3	4.0	4.9	4.4	19%
S.D.	± 1.6	± 1.2	± 1.6	± 1.5	
TNG Cons.	65	55	42	54	28%
S.D.	± 100	± 109	± 76	± 95	

fered satisfactory relief in 35.2 percent ± 2.2 percent of patients.[13] Evans found some 15 drugs which functioned as placebos to equal or surpass the ability of the nitrates to reduce the incidence and/or severity of anginal pain.[14] In that study, test patients were instructed to report subjectively "typical" chest pain experienced during their daily activities; exercise tolerance was not evaluated. In 66 patients receiving placebo therapy for more than two weeks, 27 percent showed "great improvement" with no attacks for at least a two-week period. Ten percent showed "moderately improvement," 33 percent showed no improvement, and 29 percent considered themselves worse.

Measurement of TNG consumption is often used as a means of monitoring changes in functional status during a therapeutic intervention for angina pectoris,[1,2] The reduction in TNG consumption by the patients in this study while receiving placebo therapy may have been due to a reduction in anxiety and to improved patient education. No improvement in exercise testing was noted during placebo therapy in this study yet TNG consumption and incidence of pain dropped from test to test by 15-24 percent. The placebo response in this study may be explained by a combination of factors. Anginal attacks may frequently be precipitated by levels of anxiety provoking an increase in HR and BP.[15] In this study anxiety was decreased possibly by the introduction of a strong and continuing doctor-patient relationship. The patient could ventilate his health concerns on a regular basis, receiving reassurance from a health professional. A second important factor in placebo response was the patient's experience during the series of exercise tests. The patient learned to determine more precisely what the prodromata of pain might be, and what levels of exercise could be tolerated before the onset of pain. In this study after stopping exercise TNG was given only at the patient's request or if the anginal pain did not decrease promptly. He discovered not only that the pain would go away in a few minutes without medication, but that his physician was apparently content to rely on rest rather than medication when symptoms abated rapidly. Clearly, TNG consumption did not serve as a reliable indicator of physiologic function in this study.

The reproducibility of several hemodynamic variables at the onset of chest pain in patients with ischemic heart disease has been investigated in both short and long term studies. Dagenais showed over a five day period with two tests per day that total exercise time at the onset of chest pain varied by 10.8 percent and the HR varied by 4 percent.[7] Similar results have been reported by Redwood, Robinson, and Smokler using mean testing intervals of one to thirty-three days.[3,5,10] A long-term study of the reproducibility of several variables has been reported by Blomquist, et al.[4] That study consisted of a total of 138 exercise tests over a 24-month period of time with a mean interval of 15 months between the first and last tests. Using an end-point of angina and/or ST changes he found the mean differences from test to test to be no greater than 14 percent from peak work load level, 5 percent for HR and 4 percent for HR x BP.

This study supports and extends the conclusions of others.[3-5,10] HR as measured from EKG recordings showed only a 6 percent coefficient of variation at two plus chest pain and was the most reproducible of all measurements. Therefore, following HR at the onset of moderate chest pain would appear to offer a simple approach to monitoring the long-term stability of a patient with proven angina pectoris. There was good reproducibility in HR x BP in this study with a variation of 10 percent. The slightly greater variation of HR x BP when compared with HR alone is perhaps due to the ease of measuring HR as compared with the relative difficulty in obtaining an accurate BP measurement with an external cuff during exercise. Also, the measurement itself is a product of two independent variables. In exercising normal subjects HR x BP was found, however, to be the best predictor of myocardial oxygen consumption (MVO_2) when either of these variables is varied independently.[16,17]

In this study duration of exercise was the least reproducible variable (coefficient of variation of 19 percent). Smokler, Dagenais, and Battock have demonstrated variations of 5.4 percent to 17 percent with the lowest coefficient of variation occurring in patients with long exercise times, and high coefficient of variation occurring in patients with short exercise times.[7,10,18] The principal difficulty in using "minutes of exercise," or "work performed," or even "exercise units" is that of the small numbers involved.[10] Patients with angina pectoris often do not reach four minutes of treadmill exercise before encountering two plus chest pain, and a ½ minute variation accounts for a large percentage change in exercise time. Of the 60 tests performed in this study all exceeded two minutes but 16 were terminated at three minutes or less. Only five tests extended beyond six minutes.

On the basis of the above data HR, HR x BP, and exercise time at two plus chest pain were demonstrated to be reproducible variables on repeat exercise testing over a three months period of time. This was true despite subjective improvement in some patients manifested by a decrease in TNG consumption. Of the variables measured HR demonstrated the lowest coefficient of variation with HR x BP being nearly as good. With medical intervention the product of HR x BP becomes more important, as each component may be independently altered.[6,16,17]

Previous animal studies demonstrated that the tension time index (TTI) was "the principal if not the sole determinant of myocardial oxygen consumption."[19] More recent data indicates that HR x BP correlates better with MVO_2 than the TTI in exercising normal young men in a wide variety of circumstances. HR x BP, therefore, could be of value in evaluating patients with angina pectoris.[16,17] Factors other than HR x BP appear to be involved, however, because patients develop angina at a slightly higher HR x BP product after nitrates and a slightly lower HR x BP product after beta adrenergic blockade with propranolol.[6] These differences may be due to changes in ventricular volume and/or contractility.[6] Caution must be used, therefore, when extrapolating hemodynamic data on young men to patients with ischemic heart disease. Nevertheless, since HR and BP are easily measured hemodynamic variables and demonstrate a low coefficient of variation, the product of these two variables and not TNG consumption may serve as a useful non-invasive means of monitoring therapy in patients with angina.

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Letters to the Editor

We would like to encourage physicians to contribute to the Letters to the Editor Section. We want to hear what you have to say, what you think, why you hold certain opinions. In short, we want to make this as lively and spirited a section as possible.

The Editors

Chemodectoma with Multiple Skeletal Metastasis and Anemia

Report of a Case

ROBERT A. SWEET, M.D.,[*] JOHN F. FAIRBAIRN II, M.D.;[*] JOHN W. JOYCE, M.D.;[*]
and JOHN R. GOELLNER, M.D.[*]

A chemodectoma of the carotid body was diagnosed in a 16-year-old girl and resected six months later. The patient was anemic before resection, despite iron therapy. Following surgery her Hgb returned to normal, but again dropped five years later and persisted despite extensive iron therapy. Eight years postdiagnosis, metastasis to the vertebrae, sacrum, and coccyx was found. The literature reveals that the vertebrae are a site of predilection for metastasis of chemodectoma. Radiotherapy has reduced pain in this case, but the patient's outlook remains poor.

CHEMODECTOMA, A POTENTIALLY malignant carotid body tumor, occurs infrequently enough in any given practice to warrant periodic report and review. The case reported here is of particular interest because of the early age at onset, presence in a female, metastasis and the attendant anemia, and the results of treatment for this rarely malignant lesion.

Case Report

The patient was first evaluated at age 16, in July 1966, when she presented with a non-tender neck mass that had been enlarging gradually for at least three years. Physical examination revealed a 4 by 5 cm, moderately firm mass situated below the superior portion of the right sternocleidomastoid muscle. It was pulsatile, and a loud systolic bruit was associated with it. Mild atrophy of the tongue was noted. Anemia was present, hemoglobin measuring 10.6 g/dl (normal 12-15) and serum iron 56 mg/dl (normal 75-175). Stool specimens were negative for occult blood. A peripheral blood smear showed rouleau with hypochromic microcytic erythrocytes. The sedimentation rate (ESR) was 67 mm in one hour (normal <20). Serum protein electrophoresis showed an alpha-2-globulin of 1.4 (normal 0.5-0.8). Urinalysis, chest roentgenography, urinary metanephrines, catecholamines, and vanillylmandelic acid (VMA) were normal. A right brachial angiogram showed a highly vascular mass, eight cm in greatest diameter, at the bifurcation of the right carotid artery. Surgical exploration disclosed that the tumor was firmly adherent to and invading the carotid-artery bifurcation and extending inferior to it. The tumor was considered unresectable, but biopsy specimens were reported as chemodectoma.

On a follow-up visit five months later, physical examination again revealed a right neck mass. Although the patient had been taking iron supplements orally ever since dismissal from the hospital, the hemoglobin was only 11.6 and serum iron 66. The ESR was elevated at 73. A right brachial angiogram showed a highly vascular mass at the bifurcation of the right carotid artery. It was noted that a small portion of the internal carotid artery cephalad to the tumor was free of involvement. In January 1967 (six months after the first examination) the patient underwent resection of the tumor and reconstruction of the internal carotid artery with a saphenous-vein graft. The tumor surrounded the right common and internal carotid arteries.

Follow-up in 1968 revealed no clinical evidence of tumor recurrence. Hemoglobin had risen to 12.5, and serum iron to 117; and the ESR and the findings from chest roentgenography and urinalysis were normal. In 1970 there was no clinical evidence of tumor recurrence, hemoglobin was 13.7, and urinary metanephrines and ESR were normal.

The patient did well until July 1973, when she consulted her family physician regarding menometrorrhagia. Her hemoglobin then was 9.8. Throughout the ensuing 11 months she was given iron orally and parenterally and twice underwent dilatation and curettage. Both times, the microscopic diagnosis was proliferative endometrium. Despite these measures, at the end of the 11 months the serum iron was only 40 μg/dl with total iron-binding capacity (TIBC) 225 μg/dl (normal 250-450) and saturation 16%; and hemoglobin ranged during this period from 8.7 to 9.4.

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See editorial, page 857.

The patient came again to this clinic in October 1974 because of severe pain of approximately three days' duration in the right hip and low back. A lesser degree of low back pain had been present for four months. Her weight had decreased 8.6 kg in the five months prior to readmission, and for one year she had had episodic night sweats. Physical examination revealed right ptosis with meiosis, atrophy of the right side of the tongue, and a grade 2/6 systolic ejection murmur along the left sternal border.

Initially, abnormal laboratory data included hemoglobin 9.6, leukocyte count 11,900/cu mm blood (normal 4,100-10,900) and platelet count 739,000 (normal 130,000-370 000), serum iron 17 (normal 65-170) with TIBC 232 μg/dl (normal 250-370) and saturation 7% (normal 20-50), ESR 86, alkaline phosphatase 621 U/liter (normal 76-196), gammaglutamic transpeptidase 71 U/liter (normal <50), and serum albumin 2.10 g/dl (normal 3.3-4.3). Normal findings were reported initially from urinalysis and the leukocyte differential count, and normal values for VMA, homovanillic acid, metanephrines, calcium and phosphorus, creatine kinase, lactic dehydrogenase, glutamic-oxalacetic transaminase (GOT), and alpha-1, alpha-2, and beta-globulins.

Early during hospitalization the hemoglobin continued to decrease to 8.1 while stools remained negative for occult blood. A peripheral blood smear showed hypochromic microcytic red cells with lack of regeneration. Two reticulocyte counts were 1.7 and 1.8% (normal 0.5-2.5). Bone-marrow aspirate and biopsy showed normal iron stores and distribution with reactive plasmacytosis and lymphocytosis.

Roentgenographic examination revealed destruction of the spinous process and lateral masses of C-5, destruction and collapse of L-1, and involvement of the thoracic vertebrae and sacrum (Figure 1). A bone scan showed abnormal uptake in the cervical, thoracic, and upper and mid lumbar segments, and in the sacrum and coccyx.

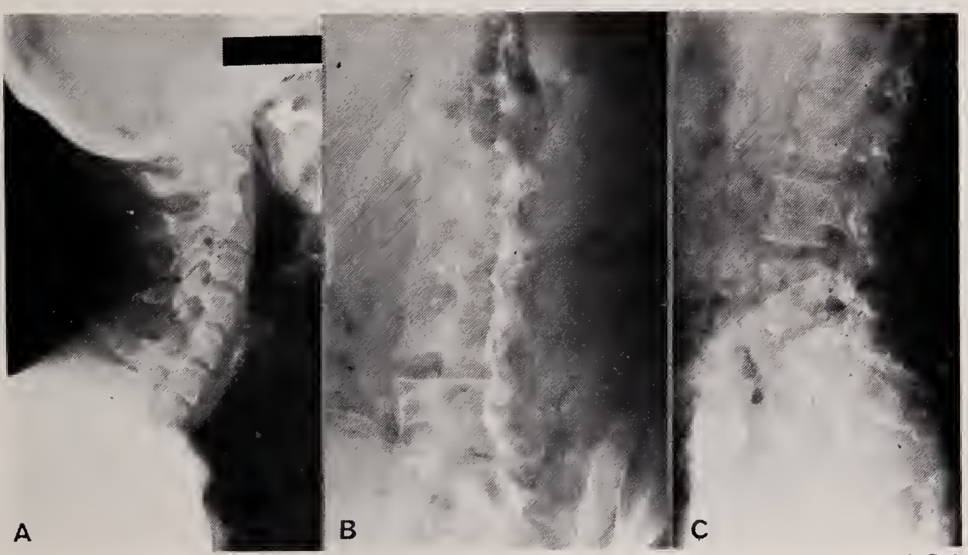

Fig. 1—Involvement of spinal column in 1974. (A) Destruction of spinous process of C-5. (B) Destruction and collapse of L-1. (C) Involvement of sacrum.

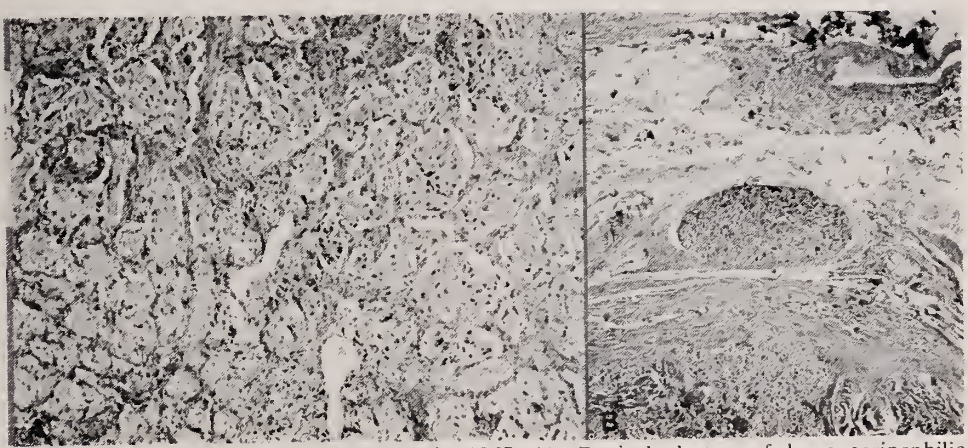

Fig. 2—Sections from tissue resected in 1967. (A) Typical clusters of large eosinophilic cells and prominent vascularity. (Hematoxylin and eosin; x100.) (B) Vascular invasion by tumor. (Hematoxylin and eosin; x64.)

Follow-up laboratory investigation disclosed that alkaline phosphatase had risen to 821, SGOT to 45 U/liter (normal 2-20), serum glutamic pyruvic transaminase to 37 U/liter (normal 9-24), and ESR to 120. Also, the pulse rate was 120/min during rest.

Open biopsy of the fifth cervical vertebra resulted in diagnosis of metastatic chemodectoma.

A total of 2,700 rads was directed to the entire vertebral column over a period of 21 days. The patient reported improvement of her back pain after the radiotherapy, but not enough time has elapsed for objective determination of improvement.

The overall hospital course was complicated by progressive anemia, which required transfusion of two units of packed red blood cells when the hemoglobin declined to 7.6. There was no evidence of occult blood loss or menometrorrhagia. Prior to radiotherapy the patient's weight had fallen to 28 kg despite adequate oral caloric intake, and it did not change afterward.

Pathologic Findings

The tumor removed in 1967 surrounded both the common and the internal carotid vessels, but the intima appeared to be intact.

Microscopically, the resected tissue and both biopsy specimens had the pattern of chemodectoma (paraganglioma of carotid body). Epithelial cells were arranged in groups or clusters, were moderately large with eosinophilic cytoplasm, and in areas showed considerable nuclear pleomorphism (Figure 2 A). Vascularity was prominent: and in the 1967 specimen, vascular invasion was evident (Figure 2 B). The first biopsy specimen (1966) and the tissue taken from the vertebra in 1974 were fibrotic but retained the vascularity and *zellballen* appearance of paraganglioma (Figure 3).

Fig. 3—Section from 1974 biopsy specimen, showing more fibrotic character, vague clustering of epithelial cells, and relation to vessels. (Hematoxylin and eosin; x250.)

Comment

The Armed Forces Institute of Pathology[1] has proposed "paraganglioma of the carotid body" as the preferred term for a neoplasm first described by Marchand[2] in 1891. "Chemodectoma" is the name suggested by Mulligan[3] in 1950 for this neoplasm, which arises from chemoreceptor cells such as those occurring in the carotid body, glomus jugulare, ganglion nodosum of the vagus, ciliary ganglion in the orbit, and aorticopulmonary body. Among these various sites, the most common location of the neoplasm is in the carotid body at the main bifurcation.

Although the malignant potential of these tumors is low, there is great divergence of opinion regarding the frequency with which they become malignant. Fanning and associates[4] reported a metastasizing carotid body tumor in 1963 and found reports of 25 others. Approximately half of the tumors had spread only to regional lymph nodes and the remainder to distant visceral sites, especially the lungs. The primary tumor usually had been present for many years before metastasizing.

Shamblin and associates[5] found that among the 500 cases of carotid-body tumor reported in the literature, 16 included local metastasis and 16 distant metastasis. The incidence of distant metastasis is about 3%. The vertebrae have been osseous sites of metastasis in nine of the cases reported and in our case (Table). In another case the tumor had spread to the ilium only. Metastasis from chemodectoma tends to be long delayed. In the eight cases with data available, the interval from diagnosis to metastasis had a range of three and a half to 15 years and a mean of 10.3, which is similar to the eight years in our case.

Overall there is no sex preponderance in the occurrence of chemodectoma;[1] yet only two of the 10 patients with vertebral metastasis were female.

Using histologic criteria alone, various authors in the 1940's and 1950's estimated the incidence of malignancy as 0 to 50%.[14-20] More recent evidence indicates that prediction of malignant potential on the basis of pathologic examination has been fruitless.[1] However, we believe that the vascular invasion seen in the 1967 specimen might have been a harbinger of the future course of our case.

The patient's long-standing anemia was noted when the primary tumor was first diagnosed. There was no evidence of menometrorrhagia at that time; and after removal of the primary tumor, the hemoglobin and serum iron values became normal. The recurrence of anemia in 1973 was attributed solely to the menometrorrhagia. However, continuous oral and parenteral iron therapy and dilatation and curettage performed twice did not resolve the anemia. During hospitalization there was no evidence of menometrorrhagia or occult blood loss, and laboratory findings suggested the anemia of chronic disease. Anemia concomitant with metastatic chemodectoma has not been reported previously; but it might be expected in a case such as this, where metastatic disease is widespread.

Surgical treatment is generally preferred for primary chemodectoma whenever feasible. However, experience with specific treatments for metastatic foci is very scanty because of the rarity of this phenomenon. Donald and Crile[6] stated that "xray therapy" produced no symptomatic relief in their patient with osseous metastasis, and similar results were observed by Pendergrass and Kirsh.[7] However, Gustilo and associates[21] reported that in their patient who had an isolated metastasis to the left ilium the symptoms were

TABLE
Reported Cases of Chemodectoma (Carotid-Body Tumor) With Vertebral Metastasis

Report	Age, sex at Dx	Location		Biopsy metas.	Yr Dx-metas.	Autopsy
		Primary	Metastasis			
Donald & Crile[6] (1948)	27, M	L carotid body	T-5, 6 Other skeletal	Yes	14	No
Pendergrass & Kirsh[7] (1947)	24, M	L carotid body	C-4, T-9, L-4 Other skeletal Liver, lungs	No	3½	Yes
Romanski[8] (1954)	50, M	L carotid body	? L-4* Lungs, heart Left 3rd rib; upper mediastinum	No	10	Yes*
Goormaghtigh & Pattyn[9] (1954)	52, M	R carotid body	L-4, L-2 Lungs	No	8	Yes
Warren[10] (1953)	?	Carotid body	T-3, T-6 Mediastinum Ribs	?	?	?
Sessions and associates[11] (1959)	15, M	L carotid body	Cervical, thoracic, lumbar vertebrae Lung Other skeletal	Yes	12	No
Brown and associates[12] (1967)	32, M	L carotid body	C-6, L-5	Yes	7	. . .
Brown and associates[12] (1967)	41, M	L upper neck	C-6, T-6 R 5th rib	Yes†	15	. . .
Say and associates[13] (1973)	45, F	R carotid body	T10-12, L2-5 Other skeletal	Yes	13	. . .
Present	16, F	R carotid body	Cervical, thoracic, lumbar vertebrae Sacrum, coccyx	Yes	8	No

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*L-4 not examined.
†Not carotid body.

relieved by irradiation. In our case the patient's vertebral pain was much decreased by radiotherapy. Certainly experience is too limited at this time to support prediction of the effect irradiation may have in future treatment for metastatic chemodectoma.

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Continuing Education

Winter Meeting—Minnesota Radiological Society, February 5, 1977. Sheraton-Ritz Hotel, Minneapolis, MN. 3rd Annual K. W. Stenstrom Memorial Lecture, David E. Kuhl, M.D., Director-Nuclear Medicine, University of California at Los Angeles. "The Present and Future of Transmission and Emission C.T. Scanning."

Minnesota Society of Clinical Pathologists Meeting, April 23, 1977, University of Minnesota, Room 2-615, Building A. Program will be published in next issue.

THERE ARE A LOT OF PEOPLE GETTING BETWEEN YOU AND YOUR PATIENT.

Medicine today is in the spotlight, subjected to all inds of scrutiny. Your control over patient therapy is eing monitored, judged and occasionally abrogated, ometimes by unknown third parties.

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Drug substitution In most states, pharmacy laws, egulations or professional custom stipulate that your on-generic prescriptions be filled with the precise prodcts you prescribe. But in the last five years, a dozen or ore State laws have been changed, permitting the pharacist in most cases to select a product of the same eneric drug to fill any prescription.

Ironically, this dilution of physician control has ken place against a background of growing evidence at purportedly equivalent drug products may be inquivalent, since neither present drug standards nor their nforcement are optimal. In fact, the FDA itself says it as not enforced the same standards for hundreds of follow-on" products that it had applied to the original DA approvals. Thus physician control over patient erapy is being eroded with a risk that patients may be xposed to drugs of uncertain quality.

The major advertised claim for substitution is reduced rescription prices for consumers. Yet no documentation f any significant savings has been produced.

MAC Maximum Allowable Cost, MAC for short, is Federal regulation designed to cut the Government's rug bill by setting price ceilings for drugs dispensed to edicare and Medicaid patients. Unless the prescriber ertifies on the prescription that a particular product is edically necessary, the Government intends to pay only r the cost of the lowest-priced, purportedly-equivalent, generally-available product. The effect of the program may be that elderly and indigent patients will be restricted to products which someone in Washington believes are priced right. Practicing doctors will have little to say about administration of the program, since Government will have absolute authority to make its choices stick.

The drug lag The future of drug and device research depends upon a scientific and regulatory environment that encourages therapeutic innovations. The American pharmaceutical industry annually is spending more than $1 billion of its own funds and evaluating more than 1,200 investigational compounds in clinical research. Disease targets include cancer, atherosclerosis, viruses and central nervous system disorders, among others. But there is a major barrier to the flow of new drugs to your patients: The cost of the research is more than ten times what it was, per product, in 1962; and whereas governmental clearance of new drug applications took six months then, it commonly consumes two years now.

The FDA needs adequate time, of course, to consider data. But it is equally clear that the present approval process contributes to needless delay of needed therapy. That's why the increased efficiency of the drug approval process is vital to all our futures.

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Editorials

Semen Analysis and Male Fertility

Dr. Posalaky* has written an informative article on the physiology of semen production and its relationship to male fertility. While information is compounding on underlying physiologic mechanisms, treatment of male infertility remains in many cases a perplexing problem. Of particular interest to those of us treating male infertility is the table relating to azospermia. By performing a fructose test on the semen and then, if indicated, an FSH determination one is readily able to determine which men with absent sperm in the semen sample are candidates for testicular biopsy. The majority of male infertility patients have oligospermia usually with associated motility defect as well. Effective treatment is perplexing. Endocrine problems are unusual (less than 10%) and in fact such tests as thyroid function are usually not performed unless there is some indication from the history or physical exam. Adequate history and physical is, of utmost importance. Missing in the article regarding history is the importance of medication which such a man might be taking. Several medications including nitrofurantoins and colchicine are known to interfere with spermatogenesis. In addition adrenergic blocking agents have been shown to interfere with contraction of the vas deferens and may produce oligo or azospermia. In fact, these agents may some day play a role in a male "pill" for contraceptive purposes. In the physical exam one checks for signs of endocrine imbalance, anatomy of the genitalia, and/or infection. In addition one must always check for a varicocele. The best hope for correction of low sperm count and motility lies in correction of a varicocele if it is found to exist. Drug treatment for oligospermia has been far from ideal but there has been some success with low dose cortisone therapy and more recently with drugs borrowed from the gynecologists' armamentarium, such as Pergonal. Nevertheless we often eventually find ourselves counseling such patients on adoption procedures but we remain hopeful that new modes of therapy will be developed to aid this perplexing area of medical practice.

William L. Engel, M.D.
Minneapolis, Minnesota

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*See page 877.

Unstable Diabetes

The majority of patients with insulin requiring diabetes are relatively easy to manage using many various regimens. The article by Lufkin in the November issue* deals with the remainder of patients whose management is more difficult. The author appropriately points out that control can often be improved by careful attention to detail. At each visit the clinician should review with the patient various aspects in management

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*Lufkin EG: Management of unstable diabetes. Minnesota Med 59:11:753, 1976.

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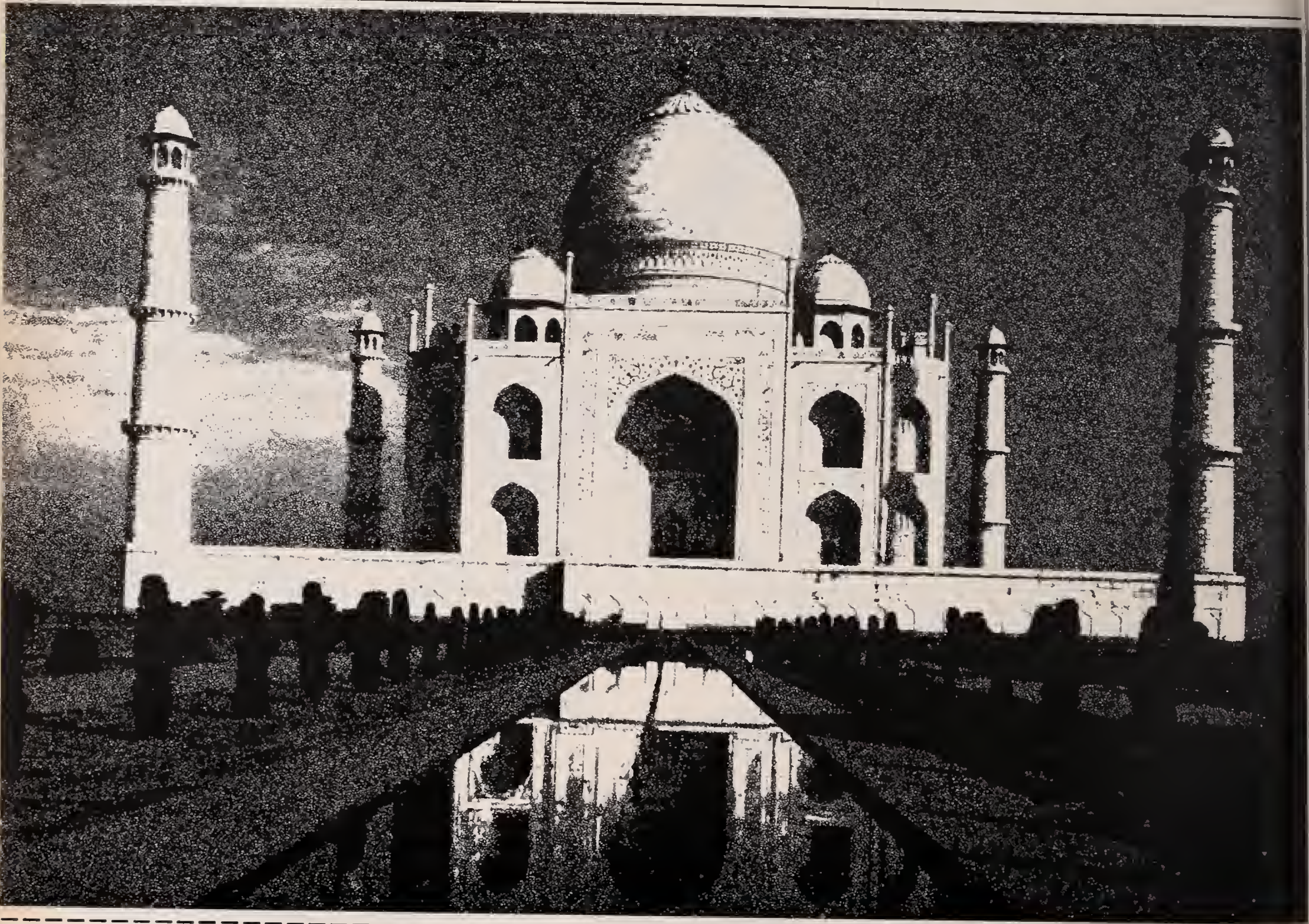

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which are too often assumed after initial patient instruction. Those points covered should include: Diet-composition, distribution and timing; insulin dosage, timing and injection technique; urine testing technique; exercise and work habits. The urine spillage pattern should be carefully reviewed for evidence of rebound or Somogyi effect.

The standard of "good control" for the unstable diabetic cannot be based on a single measurement, such as the fasting blood glucose. The patient's general sense of well-being should be considered and this includes the strict avoidance of hypoglycemic reactions. Qualitative urine testing, 24-hour urine glucose measurements, fractional quantitative urine glucose determinations and nonfasting blood glucose sampling all can be used in appropriate situations to access the adequacy of control.

Finally, the patient should understand the reasoning behind changes which are advised in management. In addition to aiding compliance this adds to the patient's knowledge of the disease and may allow independent management changes, which in turn may improve control.

William J. Bergstrom, M.D.
Minneapolis, Minnesota

Transcutaneous Stimulation for Chronic Pain Relief

STONNINGTON ET AL.* took an excellent approach to determine if transcutaneous electrical stimulation (TES) is useful in controlling pain. By classifying the patients into a "buyer" or "non-buyer" while at the same time not altering medication or given psychologic advice the results seem to bear out the transcutaneous stimulation for long term relief of pain leaves much to be desired in the vast majority of patients treated by this modality.

I would like to see the authors follow up this pilot study with another six month review to determine if the percentage of patients receiving relief drops even further.

Richard F. Galbraith, M.D.†
Minneapolis, Minnesota

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*Stonnington HH et al.: Transcutaneous electrical stimulation for chronic pain relief. Minnesota Med 59:10:681, 1976.

†Clinical Associate Professor, Neurology, University of Minnesota and Consultant, Minneapolis Clinic of Psychiatry and Neurology.

Acute Diabetic Complications

THE ARTICLE by Dr. Zimmerman in the November issue* is an excellent review article of the acute complications of the diabetic. Little can be added other than to note the exceedingly practical diagnostic and treatment recommendations advised. For the practicing physician the advice is helpful almost daily.

While diabetic ketoacidosis has been a long known entity, non ketotic hyperosmolar coma has been enlarged upon only since 1957—as noted by Dr. Zimmerman—who notes that ketoacidosis and nonketotic hyperosmolar coma form two ends of an spectrum of an entity. The reason nonketosis coma occurs in some is still not known.

Lactic acidosis is discussed as well as the rare but interesting syndrome of cerebral edema. The type of diagnosis and treatment are so practical the reader needs to note them for his current use. An excellent article.

Rudolph Ripple, M.D.
Minneapolis, Minnesota

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*Zimmerman BR: Acute Diabetic Complications. Minnesota Med 59:11:757, 1976.

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Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing. **CONTRAINDICATIONS**: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components. **WARNING**: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended. **PRECAUTIONS**: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. **ADVERSE REACTIONS**: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

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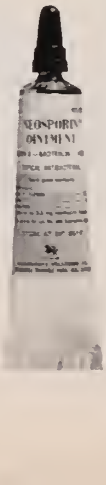

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Education of the Diabetic Patient

THE ARTICLE by Fylling et al. in the November issue* represents a model of how patient teaching programs in hospitals should be developed and implemented. While such a model may well be functional in large hospitals with personnel whose primary interest is diabetes, it may not be applicable to smaller community hospitals. In community hospitals, resources such as full time teaching nurses and dietitians and other support services may not be available. In such situations the hospital personnel may have to assume many roles and deal with many diseases so that in-depth knowledge in one area may not be feasible.

The objectives for what the person with diabetes should be taught are extensive and rightly called optimum. Questions that should be asked of such optimum objectives include: Are they attainable? Can they be measured? By what criteria can they be measured? Which objectives, or what portion of the objective must be given priority? An often overlooked area in determining objectives for patient teaching is that the objectives are most often those of the health professional and not the patient. An essential component of individualizing such objectives is to determine the goals and objectives of the learner and to blend these with the professional goals to eliminate conflict of goals. When conflicting goals are present it may decrease patient compliance with the treatment program.

The degree to which objectives are met is influenced by continuity in health care objectives as the person receives continuing care in various segments of the health care system. Frequently full progress toward the desired outcome of patient education is not achieved while the person receives care in a single segment of the system and there is a need for continuation of objectives and activities by persons in the next segment. It is essential that the objectives and the achievement towards them be communicated to the individuals in the next segment. Mechanisms for such communication should be included in every patient teaching program. Failure to include such communication may place the patient's complete educational process in jeopardy.

Lois Recker†
Minneapolis, Minnesota

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*Fylling, C. P. et al.: Education of the Diabetic Patient. Minnesota Med 59:11,789, 1976.

†University of Minnesota.

Chemodectoma

SWEET ET AL.,* in their interesting article elsewhere in this issue of MINNESOTA MEDICINE have refreshed our memories regarding a rare but fascinating tumor: chemodectoma.

They have made a nice review of the available literature on the subject. In addition, they describe a fascinating case in which recurrent chemodectoma was associated with a picture of cachexia and anemia of chronic disease.

One would hope that further studies applying newer techniques of radiotherapy and chemotherapy might demonstrate some ability on our part to control malignant chemodectoma after it has metastasized.

J. Michael Ryan, M.D.
St. Louis Park Medical Center
Minneapolis, Minnesota

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*See page 844.

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MSMA Highlights

Looking Ahead—The 1977 Minnesota Legislature

Election '76 is now history. As we look ahead to the 70th session of the Minnesota Legislature, we are asked what will be the major issues of importance to medicine and what will be the legislative climate in which our proposals, thoughts, and concerns will be received (or rejected). While Republicans may have felt they had "bottomed out" numerically in 1972 and 1974, the new legislature will represent the largest majority the DFL has held in the history of the state. Riding the crest of a heavy Carter-Mondale and Hubert Humphrey vote DFLers in the Minnesota Senate picked up a total of 11 seats and will outnumber Independent-Republicans by a margin of 49 to 18. In the Minnesota House of Representatives Republican hopes for a come back were dashed as incumbent DFL'ers lost only two seats and will continue to enjoy the more than a three to one edge they have had for the past two years. DFL'ers will outnumber Independent-Republicans by 104 to 30.

Many familiar and influential faces who have influenced legislative opinion on both sides of the aisle will be missing from the Capitol scene in January. Some chose not to seek re-election, and others lost in their bids for another term. Absent from the role call on January 4 will be such well-known Senators as: J. A. "Joe" Josefson of Minneota, Mel Hansen of Minneapolis, Rolf Nelson of Golden Valley, and the colorful Baldy Hansen of Austin, all of whom were defeated in their bids for re-election. Other influential Senators choosing not to run again included: John Olson of Worthington, Norbert Arnold of Pengilly, Jerry Blatz of Bloomington, Bob Brown of Stillwater, George Conzemius of Cannon Falls, Dick Fitzsimons of Warren, Robert North of St. Paul, A. J. "Tony" Perpich of Eveleth, and Joe O'Neil of St. Paul. Missing from the House will be well known legislators such as: Frank DeGroat of Lake Park, Howard Smith of Crosby, Ralph Jopp of Mayer, John Lindstrom of Willmar, Sal Adams of Wayzata, and Jim Ulland of Duluth who was elected to the State Senate. Several new committee chairmenships have been proposed by the DFL Senate Steering Committee. Chairmen expected to be approved by the Senate Caucus include Senator Roger Moe, Finance; Senator William McCutcheon, Taxes; Senator John Chenoweth, Governmental Operations; Senator Robert Tennessen, Commerce; and Senator George Perpich replacing Senator George Conzemius as Chairman of Health Welfare and Corrections, the Committee, through which most medically oriented bills must pass. Senator Robert Lewis is slated to chair a Finance Subcommittee on Health, Welfare and Corrections.

In the House, the Judiciary Committee has been eliminated, because of the declining number of attorneys.

It is expected most incumbent committee chairmen will be re-appointed barring a further reorganization of the committee structure. Representative Jim Swanson of Richfield will in all probability again chair the important House Health and Welfare Committee. Professional expertise in health related fields in the Senate and House will be limited to two dentists, three veterinarians, and a mortician. The only physician candidate for the legislature, Dr. Howard Mortenson of Menahga, was narrowly defeated in his second bid for a House seat as was MSMA Field Representative, Rick Teske. Two chiropractors were elected by decisive margins.

In this legislative setting what can medicine expect to contend with in the 1977-78 session? We obviously cannot anticipate all the health related issues which will be introduced. If recent sessions can be used as benchmarks, we can expect to follow or at least review more than 400 bills of concern and importance to medicine before this 70th Minnesota Legislature adjourns sine die in 1978. Some of the major issues MSMA expects to be involved in are:

Professional Liability

It is the present intention of MSMA to have introduced into the 1977 Legislature six bills which are viewed as partial remedies to the rapidly escalating costs of professional liability insurance premiums. They address the Collateral Source Rule, Periodic Payments/Revisionary Trust, Notice of Intention to Sue, Informed Consent, Standard of Care, Countersuits, and Awarding of Court Costs of Frivolous Suits.

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purchased to require a Certificate of Need. MSMA will oppose any such extension of Certificate of Need.

Death

MSMA will have introduced a bill to legalize the concept of brain death.

Chiropractic

Despite compromise legislation enacted in 1975, chiropractors are expected to introduce legislation which would allow them to draw blood, perform venapunctures, proctological exams, and other "invasive" medical procedures unrelated to chiropractic.

Cancer Quackery

MSMA will support legislation expected to be introduced by the Minnesota Cancer Society to curb the spread of cancer quackery such as the sale of laetrile and other useless substances which offer false hope to cancer patients.

Optometry

Optometrists are making efforts in some states to allow them the right to prescribe diagnostic and/or treatment drugs. MSMA will oppose such legislation if introduced.

School Health Education

MSMA will continue to support legislative efforts to incorporate programs of school health education into K-12 curriculum as the singularly most effective means of teaching and promoting preventive health care.

Family Planning

Bills to expand and develop programs of responsible contraception have been rejected by recent legislatures. MSMA will again support such legislation if introduced.

Sale of Non-Rx Products to Control Pregnancy and VD

State law restricts the sale of such articles to drug stores and other agencies dealing in health. A bill to increase the availability to condoms and other non-Rx items for the prevention of contraception and veneral disease will have Association support.

Hospitalization and Commitment Act

Efforts may be made again to amend the Hospitalization and Commitment Act to permit pre-petition screening of hospitalized patients by lay persons, thus intruding into the physician patient relationship.

Regulation of Electro-Therapy

Legislation has been suggested to regulate the physician's use of electro-therapy. If introduced again, it will be opposed by MSMA.

Highway Safety

Mandatory seatbelt usage and stricter laws to discourage driving while intoxicated will be the subject of legislative focus again with appropriate support by MSMA.

The preceding are but a small sampling of things to come. How successful we are in dealing with these and other bills will depend on several factors, not the least of which is physician involvement with their legislators at the local level. In keeping with the Association's objectives for the new Division of Socio-Economic Affairs, we will have expanded staff, a new Committee on Legislation, better research and a more effective organization generally to cope with legislative as well as other socio-economic problems. To effectively meet the legislative challenges of the 1977-78 Session, it will necessitate the commitment of doctors in every legislative district in the state. If Minnesota physicians will awaken to accept this challenge, I am confident that we can and will succeed as we look ahead towards the 1977-78 session of the Minnesota Legislature.

C. A. Anderson, M.D., Chairman
MSMA Committee on Legislation

MINNESOTA MEDICINE

The Board of Editors of Minnesota Medicine invites the members of the Minnesota State Medical Association to submit examples of their art work for publication on the cover of Minnesota Medicine. Color photographs, preferably transparencies, as well as photographs of paintings, drawings, sculpture, ceramics, jewelry, etc., are all welcome. There is no limit as to subject, but pictures of Minnesota or subjects topical to a month or season may have a slight advantage. Pictures will be returned if identified with the name and address of the maker. Please submit pictures to the Editor of Minnesota Medicine, 101 East 5th St., Suite 900, St. Paul, Minnesota 55101.

Farrell Stiegler, M.D.
Cover Editor

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(Continued to page 874)

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Precautions: Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics, or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K^+ frequently; both can cause K^+ retention and elevated serum K^+. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium® (triamterene, SK&F Co.), and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Do periodic blood studies in cirrhotics to check for nondrug-related variations in blood pictures, and in patients with folic acid depletion, since 'Dyrenium' may contribute to appearance of megaloblastosis. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

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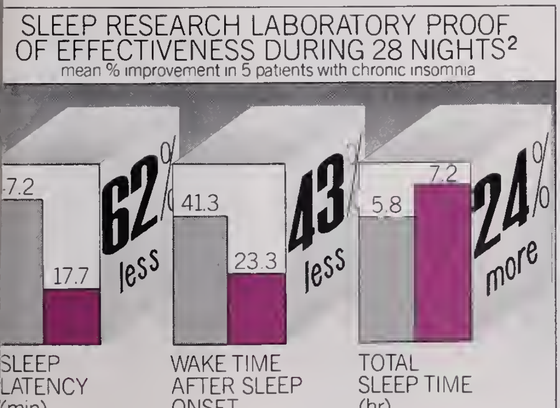

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Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.,* operating machinery, driving).

> ***Usage in Pregnancy:*** **Several studies of minor tranquilizers (chlordiazepoxide, diazepam, and meprobamate) suggest increased risk of congenital malformations during the first trimester of pregnancy. Dalmane, a benzodiazepine, has not been studied adequately to determine whether it may be associated with such an increased risk. Because use of these drugs is rarely a matter of urgency, their use during this period should almost always be avoided. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, limit initial dosage to 15 mg to preclude oversedation, dizziness and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, paradoxical reactions, *e.g.,* excitement, stimulation and hyperactivity, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase.

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REFERENCES:

1. Kales A, *et al*: *Clin Pharmacol Ther 18*:356-363, Sep 1975

2. Dement WC, *et al*: Long-term effectiveness of flurazepam 30 mg *h.s.* on chronic insomniacs. Presented at the 15th annual meeting of the Association for Psychophysiological Study of Sleep, Edinburgh, Scotland, Jun 30-Jul 4, 1975

3. Kales A, *et al*: *Arch Gen Psychiatry 23*:226-232, Sep 1970

4. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

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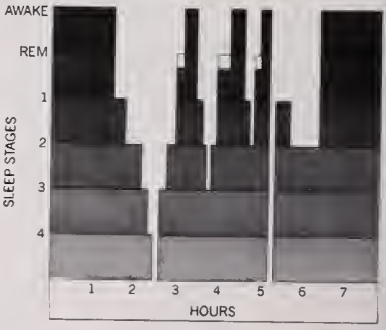

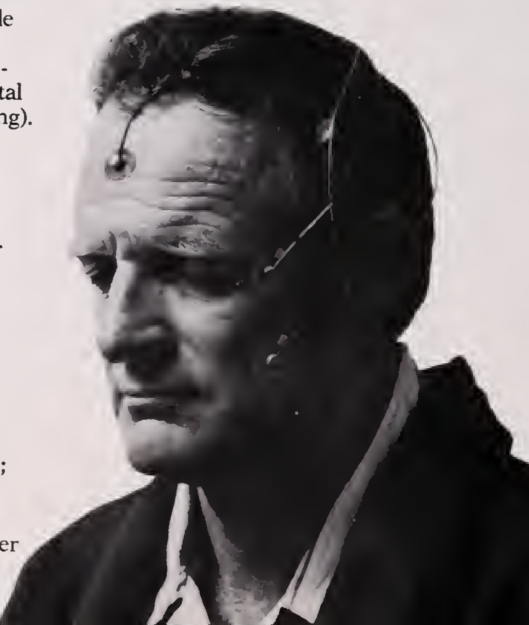

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The Practice of Medicine at Ft. Snelling 1819-1840

DAVID S. WIGGINS*

IN MARCH OF 1819 Doctor Edward Purcell wrote to his brother:

> "The intention of our government appears to Garrison the whole of our North and Northwest frontier; this with the view of cutting off British influence amongst the Indian tribes . . . Our Regiment Garrisons, three posts, one to be at the mouth of the St. Peters which shall be headquarters, and where I shall be stationed . . . You may think it strange that I have consented to go with the Regiment out of the world, as you may call it, but the fact is I go, not because I like it, but because I think I can make money".[2]

That fall Dr. Purcell did go with the soldiers of the Fifth Regiment of Infantry to the junction of the St. Peters (later the Minnesota) and Mississippi rivers. After several years of hard labor a large stone fort was erected on the bluff overlooking the rivers. Named in honor of its commandant, Colonel Josiah Snelling, this fort established an American presence in the area that effectively eliminated British control.

The soldiers were forced to rely upon temporary cabins or tents for medical facilities while they constructed a permanent garrison. By 1824 however the garrison was complete with a stone hospital, the first in the area that became Minnesota. This hospital served for nearly 20 years as the only source of white medical care northwest of Prairie de Chien. It attended to the medical needs of the men and women of the garrison, civilians in the area and any Indians who requested treatment.

Dr. Nathan S. Jarvis described the building in 1836 as follows:

> The building is stone and its whole length about 160 feet by 17 ft. 6 in. in breadth. It is divided into 9 rooms. The principle ward room is 33 feet 9 in. by 17 ft. 9 in. (sic) and is capable of containing 10 beds, but in emergency might be increased to 12 which is the full number it could possibly accommodate with a due regard to the health and comfort of the sick. Adjoining this is an extra ward room 17 ft. 9 in. by 16 ft. capable of containing 4 beds and in an emergency six. This I more particularly set apart and designed for ophthalmic and contagious afflictions, or such cases as I wished to separate from those in the general ward room. I should likewise have resort to it in a crowded state of the former. At present it is occupied with our spare bedding and bunks. The next room is the surgery which is the same dimensions as the latter, as in fact are all the remaining rooms. These are occupied with the following manner and orders. Post library, Hospital Store Room, Surgeon's quarters and post School. The Hospital Kitchen is at the further extremity of the building adjoining the general ward room . . . Beneath the building are four cellars, 2 of which are occupied by the sutler and 2 by the Hospital.[13]

Although the use of the individual rooms varied throughout the building's history, the building continued to serve as a hospital until 1840 when a new hospital was constructed on top of the post shops and the old building was torn down by the army in 1904 along with most of the other 1820 period buildings at the post.

The Surgeons and Hospital Staff

The people who staffed Minnesota's first hospital were a varied and colorful lot. The staff was headed by the surgeon, a commissioned officer ranking between a captain and a major. All surgeons were required by army regulations to be graduates of respected medical schools or colleges or have passed an examination by a board of medical officers. Thus in an age when the training of many medical practitioners was from poor to nonexistent, the surgeons who served at Fort Snelling were guaranteed to have had at least a decent medical education.

The honor of the title "first physician in Minnesota" has usually been reserved for Dr. Edward Purcell of Purcellville, Virginia. Born in Ireland and immigrating at an early age, Dr. Purcell served admirably in the War of 1812. How he planned to get rich at a surgeon's salary of $45 a month is uncertain. In any case he never got a chance to enjoy the money for he died at the post in January of 1825 from an unrecorded illness.

---

*Research Associate, Minnesota Historical Society, Fort Snelling Restoration, Fort Snelling, St. Paul, Minnesota.

Having as much claim to the title of "first physician in Minnesota" as Dr. Purcell is a Dr. Rodger Byrne who also accompanied the troops up the river in 1819. Dr. Byrne is rarely mentioned; little surprise as the only known description of him notes that he was:

> a man of science and great skill in his profession but an inveterate drunkard, and it was not uncommon occurrence, when his services were needed, to find him so stupified with liquor that nothing but a liberal dousing of cold water would fit him for duty.[14]

Dr. Byrne resigned from the army in the winter of 1820.

While none of the Fort Snelling surgeons made major contributions to medical science, several are notable for their accomplishments outside the field of medicine. Dr. Edwin James, who replaced Dr. Purcell at Fort Snelling, had served as a surgeon, botonist, geologist and chronicler in Major Stephen Long's 1819-20 expedition to the Rocky Mountains, where he was among the first party of whites to climb Pikes Peak. James desired to come to Fort Snelling so that he could beat the foreign explorers to the new discoveries to be made in the area. He complained to Washington that "the unexplored and interesting parts of our country are rapidly yielding up their treasures to foreigners."[13]

Dr. Robert C. Wood, (Figure 1) who served at the post from 1826 to 1833, successfully courted and married Ann Taylor, the daughter of then post commandant Zachary Taylor. Colonel Taylor was initially opposed to the marriage because Ann's sister had already married Lt. Jefferson Davis, later to become president of the Confederate States of America. Dr. Wood continued in the army until his death in 1869, serving briefly during the Civil War as Acting Surgeon General of the United States.

Dr. Nathan S. Jarvis, (Figure 2) whose letters provide much information about the early hospital, collected Indian curiosities from the local natives and fur traders in exchange for treatment. His collection is preserved in the Brooklyn Museum and is considered by many to be the best collection of early Eastern Plains Indian material in existence. Jarvis served as an army surgeon until his death in 1862, seeing action in both the

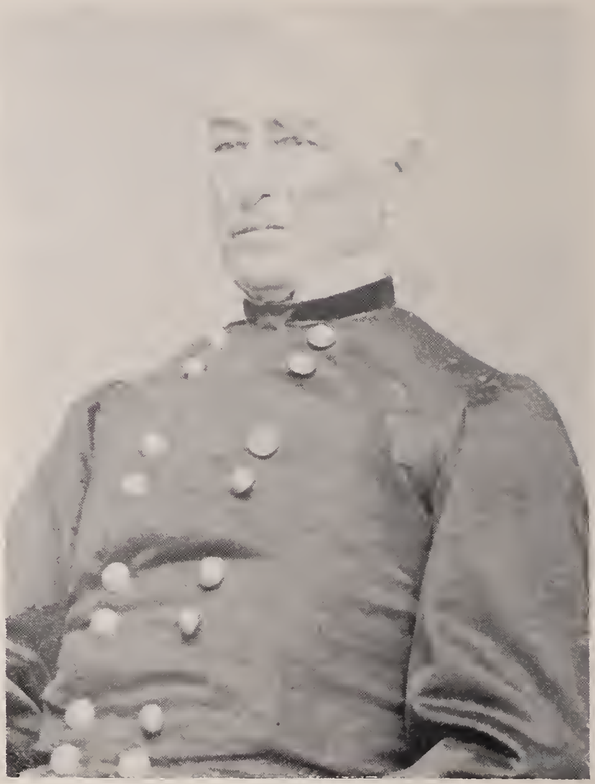

Fig. 1—Robert C. Wood, M.D.

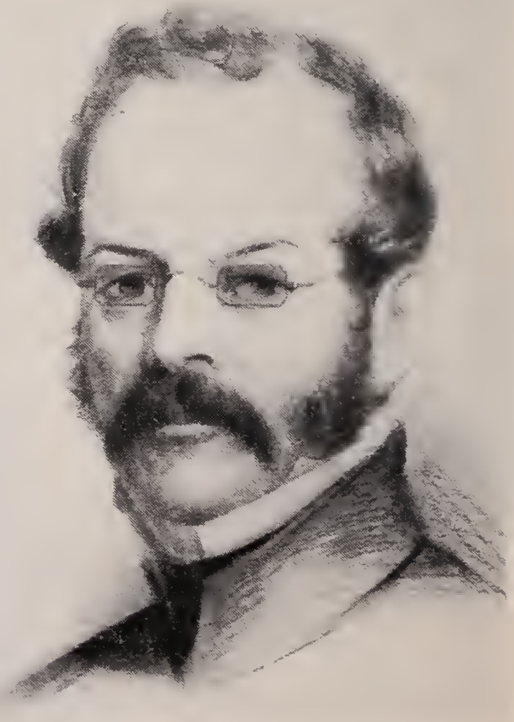

Fig. 2—Nathan S. Jarvis, M.D.

Mexican and Civil Wars.

Dr. John Emerson, who succeeded Dr. Jarvis, is best remembered as the owner of the slave Dred Scott. Scott later sued for his freedom based on his residence with Dr. Emerson at Fort Snelling in free territory. When his suit was denied by the Supreme Court, tensions ensued which contributed to the start of the Civil War. Scott's rights and Dr. Emerson's temper were behind another battle of a less serious nature.

> On a certain day in early winter when the quartermaster was distributing stoves to the officers, Dr. Emerson asked for one for his negro servant. This the quartermaster refused, saying that there were not enough in store; whereupon the doctor insinuated that the statement was a lie. Upon being insulted thus the quartermaster struck his companion between the eyes. Emerson turned on his heels immediately, but he returned in a few minutes with a brace of pistols which he pointed at his assailant. The fighting spirit of the quartermaster fell at the appearance of these weapons, and he started across the parade ground on a run followed by the doctor. A third character appeared in the person of Major Plympton, the commanding officer, who arrested Dr. Emerson . . . Not for several days was the quarrel patched up and then the terms were never made public.[6]

Usually only one surgeon was stationed at Fort Snelling at any one time, making it very difficult for surgeons to obtain furloughs. Dr. Jarvis wrote to his family in 1833 of his experience in relieving Dr. Robert Wood at the post:

> He had been here eight years without being able to get relieved. I may therefore lay aside any hope of seeing any of you for years unless I should prove more fortunate than the most of the Surgeons on Western posts. Dr. Wood was delighted in seeing me and the prospect of once more seeing civilized society from which he had been so long excluded.[4]

Most of the surgeons seemed to have found Ft. Snelling an agreeable station, albeit a bit isolated. Dr. Jarvis noted that his duties were fairly light:

> (at dawn) all turn out except sick on parade, I being the only one excused. The next call beats at 20 minutes before 7 o'clock which is the sick call when the only duty I have during the day occurs. All those who are sick or indisposed then report themselves to me at the surgery when (sic) I examine & prescribe for them or admit them to the Hospital . . . I afterwards visit the hospital & prescribe for those that are there and discharge such as are fit for duty, make an entry on the state of the weather kept by my steward & signing issues for hospital stores and rations constitutes all my labor.[4]

Other surgeons, however, particularly those from the South, found duty at the post less enjoyable. Surgeon J. P. C. McMahon, relieving Dr. Wood in 1827 for a brief furlough, bemoaned:

> Oh for the dear delightful, swampy south once more! There is something balmy and renovating in its swampy exhalations unknown to the vapid atmosphere of this Siberia. Is there no relief for the wicked or have I by my own folly closed the door against return to the lovely domains of yellow fever.[13]

The surgeon was assisted in the work of the hospital by an enlisted hospital staff. The size of this staff varied with the number of men stationed at the post but usually consisted of a hospital steward, three male nurses, a hospital cook and a matron. This staff shared quarters in a room next to the main ward described by Lt. McClure in 1833 as "a room for hospital attendants to sleep in, for lying in women and dead bodies."[12]

As enlisted men of the period were notorious for their bad character, putting together a good hospital staff was often a challenge. Surgeon McMahon while longing for the south also complained:

> I was necessitated to perform the minor and to me more harassing duties of hospital Steward. It will hardly be credited, but such is nonetheless true, that there can not be found in this Regt. a single non-commissioned officer or private possessing sufficient sobriety, capacity and honesty to fill a station of such comparative irresponsibility.

The hospital steward, ranked as a sergeant, and receiving $8 a month, was often the only member of the hospital staff who was literate or had any knowledge of medicine. He attended to medical emergencies in the surgeon's absence and one steward, Perrin Barker, was called upon to serve as the post surgeon for three months after the death of Dr. Purcell. Barker served well, performing the first recorded amputation in the area. An Indian by the name of Markpee Manee was shot while escaping from the fort where he was being held prisoner for the murder of some cattle drovers. One observer remembered the incident thusly:

> The arm had to be amputated, but the surgeon, Dr. Purcell was dead; so the sergeant of the hospital undertook the job. He tied the old man to a table and went to work, and in about two minutes the arm was off. During the operation the old man did not let on that it hurt him in the least. When

> they got through he asked if they were done. I told him he had but one arm now. 'Well, then give me a smoke' he said. He did not appear to mind what was going on any more than if they were cutting away at a piece of leather.[7]

Apparently the success of the operation was enough to convince Barker of his ability to practice, for when his enlistment was up later in the year, he absconded with a large portion of the post's surgical instruments.

The remainder of the staff had duties requiring less medical skill. The male nurses or hospital attendants attended to the everyday care of the patients. The hospital cook prepared the special diets prescribed by the surgeon while the matron, usually married to another member of the staff, was concerned principally with the hospital laundry. All received five dollars a month for their labors.

Sick and Wounded

While the officers, women and children of the post and any civilians in the area relied upon the post hospital for medical care, the majority of the hospital's business came from the garrison's enlisted men. These men were required by regulations to be between the ages of 18 and 35 and to have passed a physical examination before enlistment. The 1825 regulation reads:

> Surgeons will be particularly attentive to the examination of recruits, and suffer no man to pass who has not, at his examination, been stripped of all his clothes, in order to ascertain, as far as possible, that he has the perfect use of all his limbs; that he has no tumors, ulcerated legs, rupture, nor chronic cutaneous affection, nor other infirmity which may render him unfit for the active duties of the field; and it shall be their duty to ascertain as far as practicable, whether he is an habitual drunkard or subject to convulsions of any kind . . . Invalids having piles or other infirmity not always to be discovered by the inspecting surgeon, who impose themselves upon recruiting officers as sound and able bodied, shall previous to dismission, be put into close confinement, or other wise punished at the discretion of a court-martial as swindlers and imposters.[11]

Because of these restrictions and because of their controlled living conditions, the types of diseases and injuries affecting the enlisted men probably varied from those suffered by the civilian population. While the quarterly reports of the sick and wounded at Fort Snelling are incomplete up to 1825, the remaining reports give a good indication of the types of problems with which the hospital dealt. The following table notes the thirty most common entries in the quarterly reports of 1825 through 1839. The afflictions are listed as they appear on the reports with no attempt being made to second guess the diagnoses.[10]

Most Common Afflictions:
As they appear in quarterly reports
of sick and wounded 1825-1839

1.	Catarrh	1014
2.	Wounds	568
3.	Diarrhea	377
4.	Rheumatism	296
5.	Malaria	268
6.	Fractures and Sprains	228
7.	Colic	204
8.	Ulcers	202
9.	Rheumatalgia	146
10.	Ophthalmia	146
11.	Dysentery	120
12.	Cephelalgia	92
13.	Chilblains	90
14.	Boil	81
15.	Gonorrhea	69
16.	Pleurisy	68
17.	Remittent fever	65
18.	Vertigo	57
19.	Irritative fever	51
20.	Cholera	41
21.	Dyspepsia	36
22.	Constipation	33
23.	Intemperance	32
24.	Syphilis	32
25.	Burns and Scalds	30
26.	Eruption	28
27.	Hemorrhoids	28
28.	Debility	26
29.	Epilepsy	25
30.	Cynanche	22
All others		336
Unidentified, illegible etc.		318
Total		5110

The most sickly time for the men of the Fifth Infantry at the St. Peters was the initial winter of 1819-20. That winter a severe outbreak of scurvy killed 32 of the 230 men present before it was halted. In August of 1819 the soldiers of the fifth had arrived at the St. Peters after a difficult keelboat journey up river. The Surgeon General noted that:

> From Green Bay up the Mississippi they were not infrequently obliged to labor in the water beneath the rays of ardent sun, sleeping in their wet clothes and exposed to a damp atmosphere impregnated with Malaria, they became reduced by disease, and in this state of predisposition to scurvy they began late in the season the establishment of their winter quarters . . . They were destitute of groceries and vegetable food, except flour and corn which were more or less damaged from having been wet; and their animal food, which was prin-

> cipally salted, they were obliged to eat during a portion of the winter in a putrescent state. The condition of the meats, however was as far as practicable corrected by washing and boiling in charcoal.[2]

On January 5, 1820, Lt. Colonel Henry Leavenworth, then in command at St. Peters, reporting the illness of his men to Washington with typical concern for his reputation, in advertently pointed out the difference between the fare of officers and enlisted men:

> Our officers and their waiters and the women of the garrison have been very healthy but the men have been quite sickly. I am aware that some persons are of the opinion that the pond which I before mentioned has a prejudicial effect upon the health of the men. I do not think so, because the officers, their waiters and the women would have been affected by the miasma as well as the soldiers if it had existed.[5]

Most of the narrative accounts of the scurvy give the total number of deaths as between 40 and 70 but as these were all written years after the event their reliability is doubtful. An examination of the army paymaster's records gives a much more reliable record of the number of deaths. These records show that 32 men succumbed if all the deaths recorded over the winter resulted from scurvy.[9]

The disease was brought under control by a variety of remedies. One witness remembered that:

> Col. Leavenworth made every effort possible to arrest the disease, and he finally succeeded in doing so by administering decoctions of spruce and other vegetable productions, which were obtained by sending parties to the St. Croix and Chippway Rivers. Vinegar and other anti-scourbutics were also procured from Prairie du Chien.[1]

Another witness noted:

> as soon as the frost was sufficiently out of the ground to enable them to dig it, the Indians brought in quantities of the spignot (spikenard) root assuring the surgeon that it would cure the sick.[14]

To prevent a return of the disease, extensive gardens were cultivated to supply vegetables for the men of the post. This proved effective for the only scurvy noted at Fort Snelling after the winter of 1819-20 was an isolated case in 1825.

After 1820 the next time of unusual illness did not come until the summer of 1827. In the third quarter of that year the surgeon reported 48 cases of malaria, 25 of diarrhea and 30 of dysentery out of a garrison of 200 men. The sudden rise in these diseases is explained by a note attached to the quarterly report:

> The cases of Intermittent were obstinate tho (sic) they yielded to the bark in one or another form. They were almost all contracted at points remote from the garrison where the troops were called at various times in detachments for the suppression or prevention of Indian disturbances. The cases of Dysentery were produced by the same cause.[10]

Ft. Snelling escaped from the 1832 cholera pandemic; no deaths being attributed to the disease. Cholera actually did not reach St. Louis until October of 1832 and thus did not reach Fort Snelling until 1833. While no men died, the post did not escape without inconvenience, for at its peak, the number of men reporting with diarrhea reached 17 a day, two or three with severe spasms and vomiting. Dr. Jarvis, then post surgeon, believed the mildness of the cholera:

> due to the strict attention to diet, keeping out of the heat and wet but principally to the abstinence from the use of *spiritus liquors* and the extreme healthyness of this post.[10]

He goes on to tell of a soldier from Fort Snelling who going to Prairie du Chien: "drank freely owing to the greater facility of obtaining Whiskey at that place, was immediately attacked with Cholera and died within a few hours."

The true reason the cholera attack at Fort Snelling was so mild may be that it probably never acquired a chance to become water born. While the latrines drained directly into the Mississippi, only washing was done with river water. For drinking and cooking, water was hauled from a clear spring at Camp Coldwater, one mile up the Mississippi from the garrison.

Except for these times of illness, Fort Snelling seems to have been a healthy post when compared to the others of the period. Samuel Forry in 1842, working with the statistical information compiled by Surgeon General Thomas Lawson from the quarterly reports of 1819 to 1839, reported that:

> The total of deaths, according to the post returns, is twenty-four, the annual ration of mortality being 1.6 per cent. Of these, thirteen are reported in the medical returns, viz., one phthisis, two remittent fever, one meningitis, two gun-shot wounds, two casualties, one drowned, one suicide, and three from causes not designated. Excluding those reported from accidental causes, the average of mortality is less than .5 per cent.
>
> The relative agency of the seasons in the production of disease in general, gives in the first quarter

> 52, in the second 69, in the third 65, and in the fourth 51. Hence the mean period in which each man was reported on the sicklist, is five months.[3]

While the mean period in which each man was reported sick at Fort Snelling was about average for the 44 army posts of the period (mean of all posts, 5.9 months), the average of mortality was the best of any post except West Point.

The surgeons at the post usually attributed the health of the men to the isolation of the post and the resulting difficulty the men had in procuring excessive amounts of "ardent spirits." While the isolation of the post undoubtedly did contribute to its salubrity, the post's elevation above the mosquito infested river marshes and its good supply of fresh food and clean water also must have kept the men healthy.

Treatment

Although the treatment the men received at the Ft. Snelling hospital was from surgeons who were as well versed in medicine as any that might be found in the United States at the time, it still left much to be desired. Treatment was based upon a faulty theory of disease pathology. The surgeons at the Ft. Snelling hospital all seemed to follow to some degree the teachings of Dr. Benjamin Rush. Rush held that health was based upon the balance between stimuli and the body's reaction to it. An excess or lack of stimuli resulted in a nervous debility which caused spasms in the extreme arteries (capillaries). These spasms then manifested themselves as various disease symptoms, from fever to lesions. Much as this theory differed from the ancient humoral theory, the treatments it recommended were the same remedies of bleeding, blistering and enemas combined with the administration of drugs.

Bleeding was a mainstay in the treatment of most every disease. Surgeon Emerson noted that "the diseases occurring in this climate in the winter and spring being mostly of an inflammatory character require a free use of the lancet."[10] Exactly what a free use of the lancet could mean is indicated by the medical texts of the period which advocate bleeding up to 70 ounces at a time for some diseases.

Venesection was used for general bleeding. A band was applied above a vein in the arm or leg, the vein cut with a thumb or spring lancet and the blood allowed to flow until the desired amount had been extracted. At that time the band was removed and pressure applied to the incision to stop the bleeding. In severe cases bleeding from the jugular vein was advocated.

Cupping was used for local bleeding. Eight to twenty small incisions were first made in the area to be cupped with the spring loaded blades of an instrument called a scarificator. The inside of a cupping glass was then heated and the glass placed over the cuts. As the air inside the glass cooled it created a suction which pulled the blood out of the cuts (Figure 3).

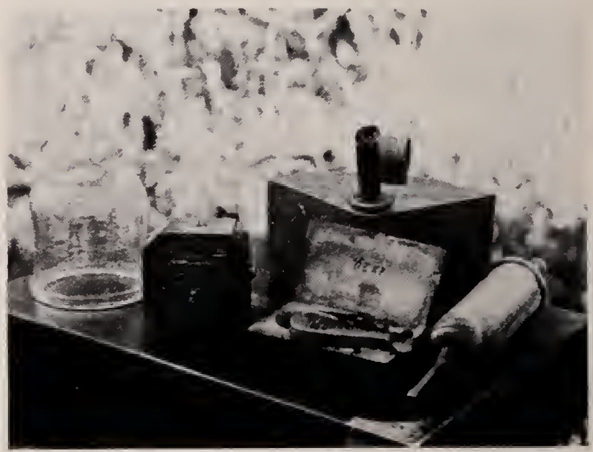

Fig. 3—Cupping glass, scarificator, cupping lamp, spring lancet and bone urethral syringe stained from the use of mercury.

Leeches were also used for local bleeding in civilian practice of the period, but they do not appear to have been used at Ft. Snelling. They may have been more trouble to get and maintain than they were worth with cupping available as a substitute.

Another mainstay of treatment was blistering. Blisters were usually raised by applying a plaster containing Melios vesicantharis, also known as blister fly or Spanish fly. This would raise blisters

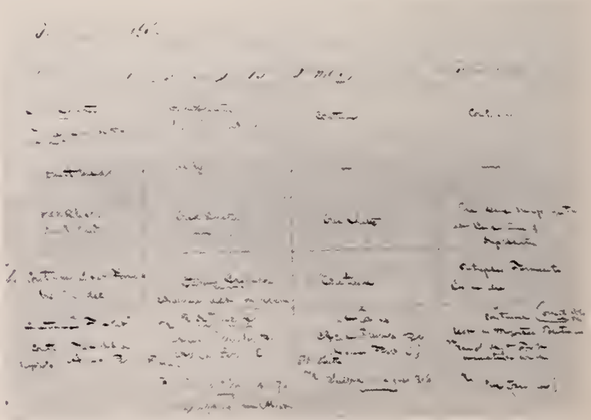

Fig. 4—Portion of an 1835 Ft. Snelling prescription book.

in about twelve hours. The blisters were then dressed for several days afterwards. The surviving fragment of the Ft. Snelling prescription book indicates that blistering was common at Ft. Snelling (Figure 4). In extreme cases blisters would be raised with caustic liquids or even boiling water.

Enemas were so frequently given in the treatment of the period that the enema syringe, not the stethoscope, was the symbol of the medical profession. Often they served as a means of administering drugs. One enema prescription of the period calls for 1 drachm of tobacco and eight ounces of water.

Drugs of some sort were used in the treatment of nearly every ailment. Sixty four different drugs were supplied the surgeons at Ft. Snelling by the army apothecary department. These were divided evenly between botanical drugs and mineral drugs, most being simple purgatives of one sort or another. The most commonly used drug was soda sulphate, a gentle cathartic. Other mineral drugs included ammonia, copper sulphate, sal ammoniac, sugar of lead, arsenic, antimonial powder, tatar emetic, several mercury compounds and nitric, hydrochloric, sulfuric and benzoic acids. Among the botanicals were Puruvian bark (and later quinine), squill, digitalis, turpentine, ipecac, senna, jalap, opium and Virginia snakeroot.[11]

Treatment usually included some regulation of diet and at times hot or cold baths, shaving of the head, or even acupuncture would be prescribed. The surgeon at Ft. Snelling in 1842 noted: "Facial Neuralgia . . . did not yield to Quinine, Blisters, . . . use of acetate morphia and Acupuncture."[10]

Fort Snelling Medicine And The Dakota Indians

Although the role the hospital and the treatment administered there played in keeping the soldiers of Ft. Snelling healthy may have been minimal, the medicine of Ft. Snelling did do a great deal towards winning for the United States the respect and allegiance of the local Dakota.

In 1832 while the east coast was succumbing to the cholera pandemic, smallpoxs had appeared among the Dakota. On May 28, 1832, Indian Agent Lawrence Taliaferro noted in his journal:

> Several of the Sioux chiefs called on me this day in a state of much alarm at the approach of the Small Pox which has reached Lac qui Parle on the St. Peters. They requested me to furnish them as quickly as practicable with vaccine matter, in which they profess to place great reliance. I told the chiefs to rest easy that I would see our surgeon & obtain a *Scab* from him if he had one to spare. If not I would write by the next express to St. Louis for a supply.[8]

Taliaferro kept his promise; by June 7 Dr. Wood had vaccinated a total of 333 Indians and Taliaferro was able to note that the "Small Pox does not seem to spread."

Surgeons at Ft. Snelling also were paid $100/year for administering everyday treatment at the Indian Agency. Although the Indians may have been impressed with white medicine, at least for one surgeon the feeling was not mutual; Dr. Jarvis wrote:

> I have obtained such influence among the Sioux by affecting cures among them as to induce their doctors, for they have regular doctors if not M.D.s among them to use my medicine with their patients, a thing before unknown among them, for these quacks; and errant quacks they are; have heretofore pretended to heartily despise our remedies and impress the Indians with the most unbounded faith in their charms and incantations. In these latter, with the exception of occasionally scarifying and drawing blood by this means consist the whole secret of of their practice . . . I have also obtained a great character among them by foretelling the lunar eclipse that took place a short time since.[4]

By impressing the Indians with the power of white American medicine, the Ft. Snelling hospital helped the post accomplish its purpose of winning their allegiance from the British.

The Restoration

Although the original hospital was torn down in 1904, visitors to the Ft. Snelling Restoration may see a reconstruction of the original on the same site, administered by the Minnesota Historical Society. The building is furnished like the original and used to interpret the history of Medicine at Fort Snelling with exhibits and living history demonstrations. The Restoration is open May through October with an admission charge of $1.00 for adults and 25¢ for children six to 16.

References will be found on page 886.

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(Continued from page 862)

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(Continued on page 888)

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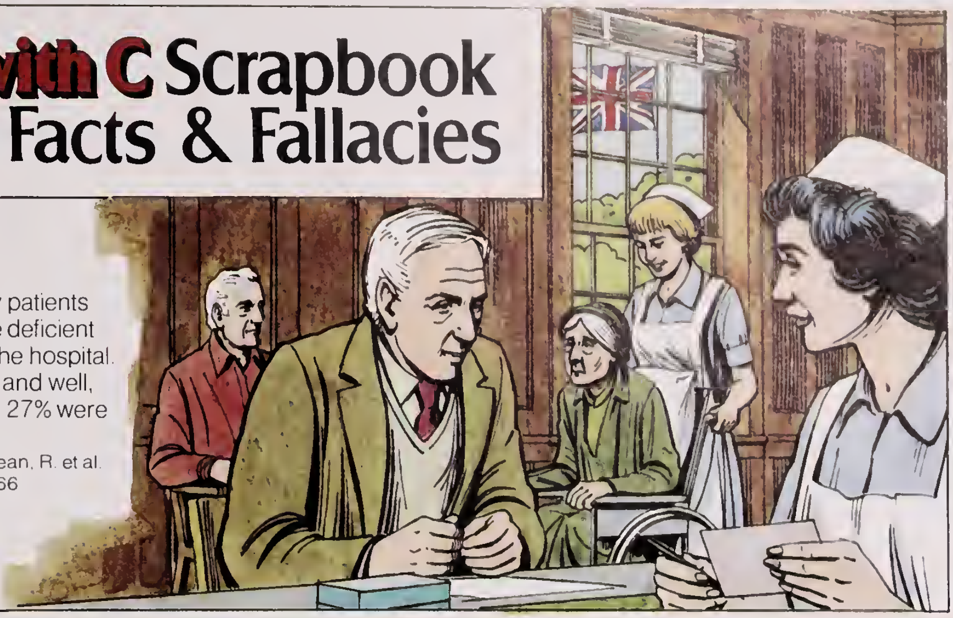

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Griffiths, L.L., Brocklehurst, J.C., MacLean, R. et al. *Diet in Old Age*, Brit. Med. J., 1:739, 1966

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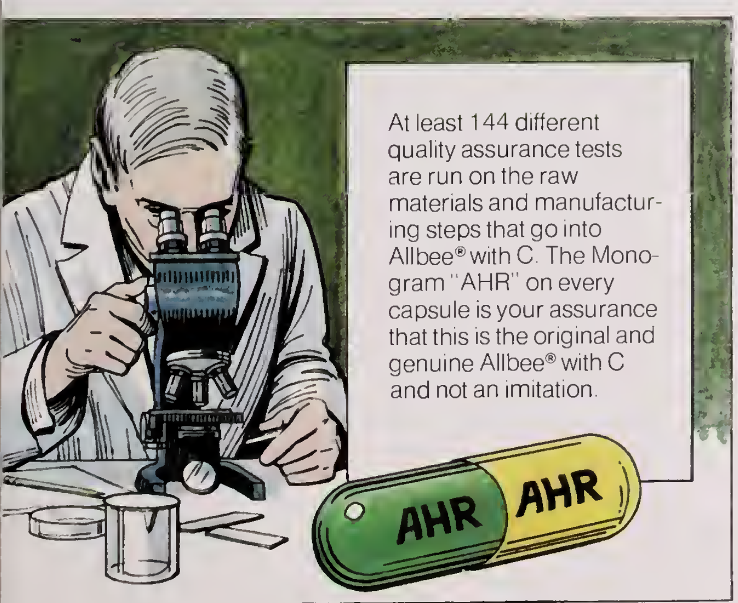

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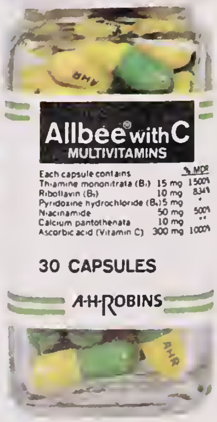
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A.H. Robins Company, Richmond, Va. 23220 A-H-ROBINS

Spasm reactor?

Donnatal®!

	each tablet, capsule or 5 ml tsp of elixir (23% alcohol)	each Donnatal No. 2 Tablet
Phenobarbital (warning: may be habit forming)	(¼ gr) 16.2 mg	(½ gr) 32.4 mg
Hyoscyamine sulfate	0.1037 mg	0.1037 mg
Atropine sulfate	0.0194 mg	0.0194 mg
Hyoscine hydrobromide	0.0065 mg	0.0065 mg

Indications: Based on a review of this drug by the NAS/NRC and/or other information, FDA has classified the following indications as possibly effective: adjunctive therapy in the treatment of peptic ulcer; the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis. Final classification of the less-than-effective indications requires further investigation.

Brief summary. Contraindicated in patients with glaucoma, renal or hepatic disease, obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy) or a hypersensitivity to any of the ingredients. Blurred vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur at higher dosage levels, rarely at the usual dosage..

A·H·ROBINS A H Robins Company Richmond Virginia 23220

Review

Semen Analysis and Male Fertility*

ZOLTAN POSALAKY, M.D.†

This review first deals with how semen is formed and discusses the importance of the different parts of the male sexual organs in this process. The second part describes how semen is analyzed; the importance and chemical value of each step is discussed. The most important part of semen analysis is the qualitative and quantitative evaluation of spermatozoa. The third part summarizes the pretesticular, testicular, post testicular causes of male infertility and their effect on spermatogenesis and semen quality. It clearly shows the necessity of a thorough personal history and examination of the patient with an infertility problem.

LIMITING POPULATION GROWTH has become a major theme in developing social and economic policy over the past decade. If we accept that no nation attempting to achieve social and economic progress for its citizens can accommodate the present trend of population increase, the significance of the male fertility problem may seem very remote. This question, however should not be looked at on a purely statistical basis. This is an important problem for those families who cherish the idea of having their own children.

To be considered fertile, a man must be capable of: (1) producing adequate numbers of normal spermatozoa in his testicles and (2) ejaculation.

Formation of Semen

The formation of semen involves the production of spermatozoa (in testis), transportation (through epididymis and vasa deferentia), storage (in the vasa) and the act of ejaculation.

Spermatogenesis is a complex and well regulated process which occurs in the germinal epithelium of the testis (Figure 1). The duration of spermatogenesis—the interval between the first spermatogonial division and the appearance of mature spermatozoa in the lumen—is 74 ± 4 days in man.[5] This time span is important because everything which affects spermatogenesis may become apparent in the semen later (maybe one or two months).

Also situated upon the basement membrane of the seminiferous tubules are the large *Sertoli cells*

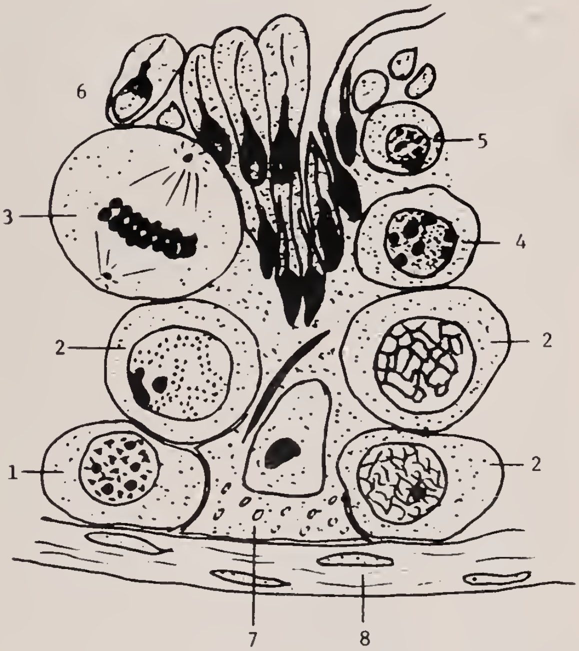

Fig. 1—Spermatogenesis: The germinal epithelium is inside the seminiferous tubule (8) of the human testis. After divisions the spermatogonium (1) developes into the primary spermatocyte, which after a long meiotic division (2: prophase, 3: reductional division) gives rise to secondary spermatocyte (4) and to the spermatides (5). These cells are developing into spermatozoa (6) (spermiogenesis). The spermatogenetic process is supported and probably regulated by Sertoli cells (7).

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See editorial, page 853.

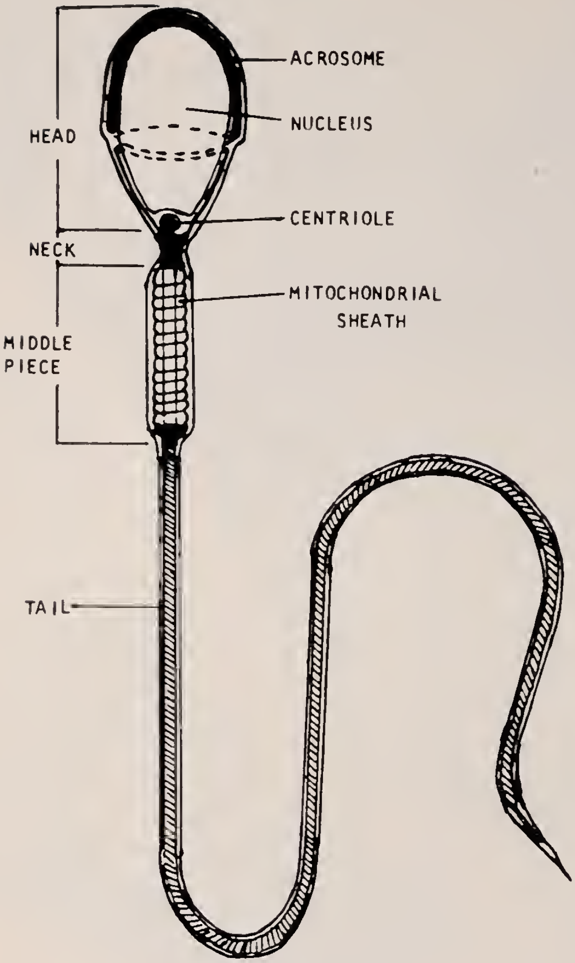


Fig. 2—Human spermatozoa.

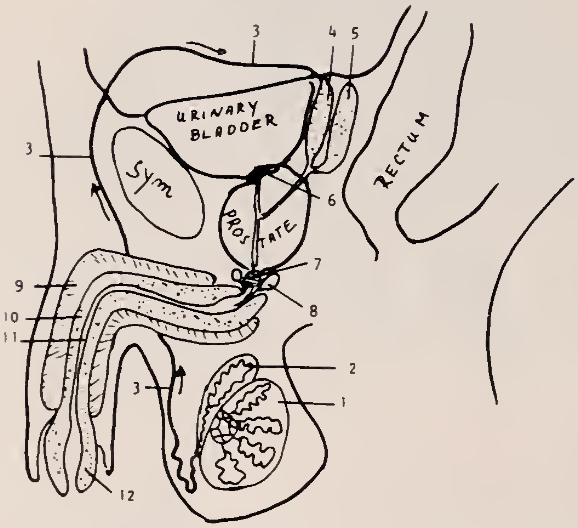


Fig. 3—Male genital organs. 1: testis, with seminiferous tubules and rete testis, 2: epididymis, 3: vas deferens, 4: ampullary portion of vas deferens, 5: seminal vesicle, 6: internal urethral sphincter, 7: external urethral sphincter, 8: Cowper's gland, 9: corpus cavernosum, 10: corpus spongiosum, 11: urethra, 12: glans penis.

with their numerous extensions that envelope the germ cells (Figure 1). On the basis of this structural arrangement, and our previous work[9,10] we believe that the Sertoli cells play the central role in the intratubular regulation of spermatogenesis. It is also understandable that any functional or structural impairment of Sertoli cells causes a release of immature or abnormal germ cells into the spermatic ducts.

The process of sperm formation is under endocrine control and it seems certain that the spermatogenesis in man can be maintained only if both FSH and LH are available simultaneously in a ratio favoring LH.[1,4,6,7]

The spermatozoa are shed into the lumen of seminiferous tubules and conducted through the canals of the rete testis and the efferent ductules (Figure 3). The sperm are motionless at this stage, and must be moved along passively either by contractile movement of the tubuli or by fluid flow.

The 9-15 collecting tubules of rete testes unite to form the *epididymis,* (Figure 3) which is a tube about 20 feet long, coiled and condensed into a structure less than two inches in length. Within the ductus epididymis—mainly in the head and the body—spermatozoa undergo maturation associated with the migration of the cytoplasmic droplet from the neck of the spermatozoa to the distal end of the mid-piece, resulting in an increased capacity for motility and fertility. This process is dependent on the endocrine activity of the Leydig cells.[6,7] Mature spermatozoa (Figure 2) are stored, prior to ejaculation, in the tail of the epididymis and vas deferens with the vast majority in the ampullary portion (Figure 3).

Spermatozoa live within the ductus epididymis for a much longer time than they do in the female reproductive tract or in vitro (30-70 days in different animals). After prolonged periods of abstinence from ejaculation the ejaculate often contains a high proportion of dead and senescent spermatozoa, and it is possible that such ejaculate could be a cause of embryonic death. The spermatozoa remain inactive within the epididymis and are transported through the duct by peristalsis aided by the increasing diameter of the lumen. The time required for the passage through the epididymis appears to be about two weeks (one to 21 days) and is influenced by the frequency of ejaculation. The *vas deferens*—a thickened muscular tube—runs up from the tail of the epididymis and behind the bladder and enlarges into the ampullary portion (Figure 3). The *seminal vesicles* (Figure 3) arise embryologically as outgrowths of the vas deferens at the ampullary portion. The duct then penetrates the prostate and opens into the urethra between the internal and external sphincters (Figure 3).

At *ejaculation* spermatozoa are mixed with the seminal plasma which derives from the secretions of the accessory genital glands. About 30% of seminal plasma originates from the prostate, approximately 60% from seminal vesicles and 5-10% from the epididymis, ampullae, bulbourethral glands and urethral glands (Figure 3). The chemical composition of seminal plasma is highly different from that of other body fluid.[8]

Different portions of semen usually follow one another in a definite sequence. Ejaculation begins with a scant secretion of Cowper's glands which acts as a lubricant, followed immediately by secretions from the prostatic gland containing the bulk of the acid phosphatase and other enzymes (muramidase, GOT, GPT, LDH, etc.) as well as citric acid, zinc and magnesium. This prostatic secretion is joined by products of testis, epididymis and vasa deferentia which have accumulated within the ampullary portion of the vasa. This early or *first portion of ejaculate* (Table 2) contains the highest concentration of spermatozoa. The last or *second portion* (Table 2) contains mostly the product of seminal vesicles with high concentration of fructose and also prostaglandin. Products of these two systems become more or less mixed and form what is called *semen*.

Normally during the process of ejaculation reflex action causes the internal sphincter (Figure 3) to close (by sympathetic activity) and the external sphincter (Figure 3) to open (by parasympathetic activity) and ejaculate is forced outward through the urethral meatus.

Semen Analysis

It is important to understand the aim and limitation of the analysis. The function of the testis can be analyzed through qualitative and quantitative analysis of spermatozoa. Several functional parameters of the spermatozoa (e.g. metabolism) are, however, not accessible to study in the clinical laboratory. The important genetic factor in the spermatozoa is also not available for examination.

There is no method available today for evaluation of epididymal function and the secretory capacity of the prostatic gland and the seminal vesicles is not closely related to male fertility. Therefore the most important part of the semen analysis is the qualitative and quantitative evaluation of spermatozoa (Table 1).

The most satisfactory *specimen* is that *collected* in the physician's office or the clinical pathology laboratory by masturbation. This allows a complete examination of the process of coagulation and liquefaction, and also eliminates the possibility of cold shock. Less satisfactory but acceptable are specimens obtained in the patient's home by coitus interruptus or masturbation and delivered soon (within one to two hours) thereafter to the laboratory. The specimen may be collected in a wide mouth clean (detergent free) glass jar supplied by the laboratory. Rubber condom should not be used because it contains substances that will kill spermatozoa. If the condom is used, it must be washed with soap and water, rinsed and dried completely. The Milex seminal pouch (Milex products) is quite satisfactory, in our experience, for semen collection.

Five days *abstinence* is recommended, but three to seven days is an acceptable range. Both volume and sperm density decrease when the frequency of ejaculation exceeds that of one every third day.

The specimen must not be cooled (below 60°F or 18°C), or warmed (above 102°F or 40°C). The collecting jar must be prewarmed. Extreme temperature changes markedly influence the motility of spermatozoa.

At or immediately after ejaculation seminal plasma is in a coagulated form. *Coagulation* results from the formation of a fibrin clot by the action of a prostatic clotting enzyme on a fibrinogen-like precursor formed by the seminal vesicles. Therefore the semen from males with bilateral congenital absence of the vasa deferentia and seminal vesicles fails to coagulate because of the absence of the coagulation substrate.

After 10-20 minutes the coagulum will spontaneously *liquefy*, the action of fibrinolytic enzymes of prostatic origin. Liquefaction should be complete within 30 minutes.

After liquefaction the semen remains viscous. *Viscosity* is, a different phenomenon from coagulation and the two forms should not be confused.

TABLE 1
Semen Analysis

Abstinence	5 (3-7) days Long abstinence → senescent spermatozoa
Collection	Masturbation (coitus interruptus)
Coagulation	Immediately after ejaculation (sem. ves.)
No coagulation	Congenital absence of vasa and seminal vesicles
Liquefaction	Complete within 20-30 minutes (prost. enzyme)
Viscosity	
Normal	Can be poured drop by drop
High	Post coital test for migration = good = no therapy poor = (1) split ejaculate (first portion for artificial insemination) (2) mucolitic detergent
pH	7.2-7.8 (increases with time!)
Volume	~3.5 ml (60% seminal vesicles, 30% prostate, 10% others)
Abnormal	>5 and <1 ml (often ▼ count) high volume = treatment; split ejaculate (first portion for artificial insemination) low volume = Leydig cell failure (?)
Agglutination	High adherence (inflammation, e.g. prostatitis) Low antiagglutinin activity (ascorbic acid treatment) Immunologic sperm agglutination test In male: autoantibodies (e.g. testicular disease, inflammation or occlusion of ducts and/or accessory glands) Treatment: Testosterone azoospermia (?) In female: Antispermatozoal antibody Treatment: Use of condom until titer decreases
Sperm density	40-250 million/ml = normal <20 million/ml = oligospermia <10 million/ml = pregnancy unlikely No sperm = azoospermia (see table 3)
Sperm motility	Progressive ≥60% 1-2 hours Poor motility = Leydig cell failure (?), cold shock (?)
Sperm morphology	≥70% with normal configuration

Although the semen analysis provides information about the composition and characteristics of semen, the most important part, however, is the qualitative and quantitative evaluation of spermatozoa.

TABLE 2
Split Ejaculate

	First portion	Second portion	Remark
Cell count	high	low	in 80% of patients
	same	same	in 5% of patients
	low	high	in 6% of patients
Viscosity	low	high	
Motility	better	worse	
Morphology	better	worse	

The first portion of the ejaculate has a better quality in most patients.

There is no demonstrable relationship between prostatic fibrinolysin content and subsequent residual viscosity after liquefaction. The viscosity of the semen can be adequately assessed by slowly pouring the specimen from the collection bottle into a small glass measuring graduate. It should flow freely and be capable of being poured drop by drop. A specimen with increased viscosity cannot be poured freely but remains a thick glob, which cannot be fractionated, and may be poured out of the container in a semi-solid mass. In general, high seminal viscosity does not in itself produce fertility problems, unless it is accompanied by poor sperm motility.

The *pH* of prostatic fluid is acid and the seminal vesicle secretion is alkaline. The pH of semen (normal 7.2-7.8) thus reflects the relative proportions between these two secretions. Although pH increases with time, it does not vary to any significant extent in relation to semen quality.

The volume of normal semen averages from 2 to 4 ml. Volumes of less than 1 ml. or more than 5 ml. are often accompanied by low sperm counts per ml.

Microscopic-Examination

A great deal of information can be gleaned by examining a drop of semen on a glass slide with a cover-slip under the dry, high power lens of the microscope. One can get a good approximation of the density of the sperm count, and the type of motility, and morphology present. If the specimen has been standing for some time before it is examined, large numbers of needle-shaped colorless spermine-phosphate crystals will be noted. The spermine in the semen comes from a prostatic secretion. It has medico-legal significance because the identification of human semen is based on the identification of derivates of spermine. The crystals are the result of interreaction between spermine and phosphoric acid, which is accumulated gradually by the action of the seminal phosphatases on organic phosphorous compounds.

Small *aggregates of spermatozoa* (three-10 cells) may also be observed during initial microscopic screening of almost all semen specimens, and is likely due to adherence to occasional leukocytes or histiocytes. These can be regarded as nonspecific agglutination. The presence of *larger aggregates* should not be regarded as a normal finding in a well mixed specimen. This agglutination can be due to an increased adherence of spermatozoa to other cells or to an antigen-antibody reaction. The first type is commonly associated with inflammatory conditions in the accessory genital glands but it is not known why only some patients with prostatitis, show a marked agglutination of spermatozoa in semen. Probably the nature of the infection plays an important role. Another cause of agglutination can be the inadequate antiagglutinin activity of the semen. There is an antiagglutinin present in the semen which exists in both an oxidized and a reduced state, but it is active only when in the chemically reduced state. When reduction fails to take place, relatively poor anti-agglutinin activity is noted. Ascorbic acid (which is normally present in the semen) has been found to be most effective for the treatment of this condition (in doses of 200 mg three times daily) with reappearance of a normal semen picture and motility in many cases.

If this therapy fails, then there is a possibility that the underlying cause is an *autoimmune phenomenon,* based upon an, as yet, poorly understood antigen-antibody reaction. The occurrence of antibodies to spermatozoa both in males with semen abnormalities and in females of infertile marriages has been established by extensive investigations during the past two decades.[12]

In the *male* several factors are probably responsible for the initiation of autoimmunity against spermatozoa: testicular diseases, inflammation of the epididymis and accessory glands and unilateral or bilateral occlusions of the ductus deferens. In the *female* the vaginally deposited spermatozoa can possibly provide an antigenic stimulus resulting in the elaboration of circulating anti-spermatozoal antibodies, in susceptible women.

Various techniques have been described for *detecting antibodies to spermatozoa* including agglutination, immobilization, precipitation, complement fixation, passive hemagglutination, immunofluorescence and cytotoxicity. Most of these techniques, however, have not yet proved to be technically reliable. The sperm agglutination test by Franklin and Dukes[3] is fairly simple and used in many clinical correlative studies. The existence of an autoimmunity is determined by mixing the patient's serum and sperm and incubating for four hours at 37°C. Similarly the presence of antispermatozoal antibodies, in the wife, can be determined by mixing her serum with the patient's sperm and again incubating at 37°C for four hours. The form of agglutination is mostly tail-to-tail but head-to-head clumping and mixtures of both types can occur. Antispermatozoal antibodies can also be present in the cervical mucus. The post coital cervical mucus (Sims-Huhner) test is suitable to screen for the presence of antibodies, for the general quality of the cervical mucus, and the ability of the spermatozoa to penetrate it.[2]

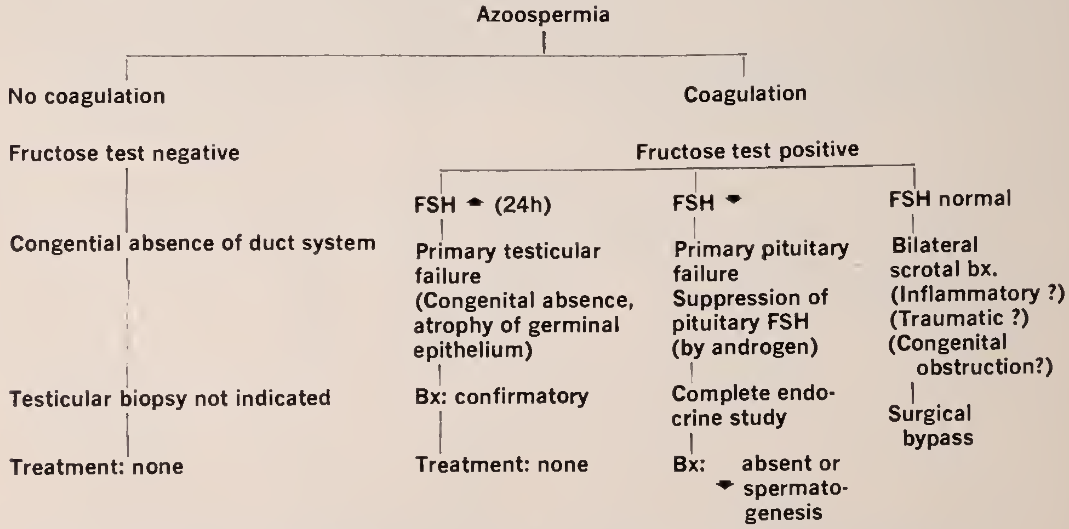
The chief method of *treating infertility in women with serum antibodies* against spermatozoa has been the use of condoms by their mates until the antibody titer declines markedly or drops to nondetectable levels. After this, unprotected intercourse is permitted with careful timing to ovulation. *For the man* with serum and seminal autoantibodies Schoysman has recently[11] offered promising therapy. Seventeen positive men were given testosterone injections which suppressed spermatogenesis, caused azoospermia, and presumably eliminated the source of the stimulating antigens. This resulted in a decreased antibody titer and upon hormone withdrawal normal semen quality returned in nine of the men with five becoming fertile.

The sperm *counting* is performed in a manner very similar to the laboratory method of performing blood cell counts, using a sperm immobilizing solution. The precision of this hemocytometer method is not very good, but, in the hand of a careful technician, the variation can be kept between 10-20%. This is an inherited error of this method, and therefore it is best to examine more than a single specimen to estimate the level of a patient's sperm production. The accuracy of the count diminishes in the severely oligospermic range below five million/ml. When sperm counts are under one million/ml it is not only impossible, but also unnecessary to obtain a count with this method. The exceedingly viscous specimen may be diluted in 1:1 ratio with Alevaire (a mucolitic agent made by Winthrop Lab).

The *minimal normal value* for the sperm count is not a definite figure, but it has been placed around 40 million/ml or 125 million total per ejaculate provided that the motility and morphology are normal. MacLeod, who has probably the greatest experience, considers that the *true oligospermia* is represented in counts under 20 million/ml.[6,7] So long as any normal motile sperm are present, no figure can be set below which pregnancy can not be achieved, but as the sperm count decreases, there is a corresponding decrease in the likelihood of conception, and when the sperm count is less than 10 million/ml it is unlikely, but not impossible that pregnancy will occur. In the case of azoospermia (no spermatozoa in the semen) the suggested workup is summarized in Table 3.

Of more importance than the sperm count itself is the *activity* or *motility* of the spermatozoa.

TABLE 3


Azoospermia
No coagulation
Coagulation
Fructose test negative
Congential absence of duct system
Testicular biopsy not indicated
Treatment: none
Fructose test positive
FSH ↑ (24h)
Primary testicular failure (Congenital absence, atrophy of germinal epithelium)
Bx: confirmatory
Treatment: none
FSH ↓
Primary pituitary failure
Suppression of pituitary FSH (by androgen)
Complete endocrine study
Bx: absent or ↓ spermatogenesis
FSH normal
Bilateral scrotal bx.
(Inflammatory ?)
(Traumatic ?)
(Congenital obstruction?)
Surgical bypass

In case of azoospermia the observation of coagulation and the result of the fructose test are valuable aids in the further workup of the patient. Bx: Biopsy

A small drop liquefied semen is placed on a prewarmed slide and covered with a coverslip. The sperm are observed under high dry magnification, and, focusing up and down, the per cent of active spermatozoa in many fields can be estimated. The percentage of sperm showing active progressive forward motion should be recorded. The speed of the forward progression can also be estimated, rated 0 to 4, but this is very subjective. When observed two or three hours after ejaculation, at least 60% of the sperm should have vigorous motility with good forward progression. When the specimen is kept in a glass container at room temperature there is a slow but definite decline in the motility so that at the end of 24 hours only a rare motile sperm is seen.

After the initial examination there is no need to make repeated observations on the in vitro specimen because this is probably of no clinical significance. The reason is that such activity in the glass container over a period of hours cannot possibly be compared with the type of activity these cells will exhibit after they have been deposited within the vagina. In the in vivo circumstances the seminal plasma is not a medium for the spermatozoa beyond a period which probably is limited to minutes. In normal intercourse the spermatozoa do not reach the main bulk of the seminal plasma in the urethra until the moment of ejaculation. There is also no evidence, in man, that the seminal plasma gets beyond the external os of the cervix. There is good evidence, however, that the spermatozoa reach the cervical mucus within one and half minutes after ejaculation and their motile existence in the vagina (in mixture of seminal plasma and vaginal secretion) cannot (be-

TABLE 4a
Male Infertility

a) Pre-testicular causes: (~11%)
Hypopituitarism:
Pre-pubertal onset:
(1) Organic (tumor, cyst, trauma) → immature testis
(2) Genetic: Hypogonadotropic eunuchoidism
a) FSH and LH deficiency → Absent ejaculation,
pre-pubertal testis
b) FSH normal, LH deficiency
"Fertile eunuchs" with some testicular development
Seminal fluid with few sperm
Post pubertal onset:
Organic: tumor (adenomas, craniopharyngioma)
Testicular hyalinization →
→ Oligo or azoospermia (with low volume)
Estrogen excess:
Endogenous: Hepatic cirrhosis, adrenal cortex tumor,)
Sertoli-tumor, interstitial cell tumor)→
Exogenous: Estrogen administration (Ca of prostate))
→ pituitary suppression →
→ testicular failure →
→ oligo or azoospermia (low volume)
Androgen excess: Adrenogenital syndrome (17-ketosteroid ↑)
Androgen producing tumor
Pre pubertal: immature testis
Post pubertal: Oligo → azoospermia,
small, flabby testis
Glucocorticoid excess:
Endogenous: Cushing's syndrome
Exogenous: Treatment for ulcerative colitis, rheumatoid arthritis,
chronic asthma
→ Oligo-spermia
maturation arrest
Hypothyroidism: ↓ Gonadotrophins → oligo-spermia
Diabetes mellitus: Arteriosclerosis of the testicular arteries →
→ Hypospermatogenesis → oligo-spermia
Diabetic neuropathy → impotence

A variety of diseases, certain inherited or exogenous factors influence the quality of semen. FSH: Follicle Stimulating Hormone, LH: Luteinizing Hormone, GH: Growth Hormone, 17 KST: 17-ketosteroid.

TABLE 4b

Male Infertility

b) Testicular causes: (~75%) ← Factors affecting fertility (spermatogenesis):

Maturation arrest: (~32%) ← Elevated temperature:
arrest of spermatogenesis
(spermatocyte-stage)
urinary GH, 17 Kst. normal
Oligo- or azoospermia

Hypospermatogenesis: (~23%)
proportional hypoplasia of all germ cells
urinary GH, 17 Kst. normal
Oligospermia ("stress pattern")

Absence of germ cells: (~8%)
"Sertoli cell—only syndrome"
(pt. potent but infertile)
urinary FSH ↑, 17 Kst. normal
Azoospermia

Klinefelter's syndrome: (~5%)
tubular sclerosis
urinary GH ↑, 17 Kst. normal
75% positive chromatin pattern
Azoospermia

Cryptorchism: (~3.6%)
(1) Malformation of the fasciae of the inguinal canal → respond to treatment
(2) Insufficient gonadotropin stimulation → respond to hormonal treatment
(3) Inherent defect in the testis, after puberty: hyalinization
urinary FSH ↑, 17 Kst., LH normal
Azoopermia

Irradiation damage: (~2%)
Progressive loss of germ. epith., sclerosis
Sertoli, Leidig cells remain
(recovery possible, 4 yrs.)
urinary FSH ↑, 17 Kst., LH normal
Oligo → Azoospermia

Mumps orchitis: (~1.5%)
Before puberty: recovery
At puberty or during adult life:
Loss of germ cells, hyalinization
(May be 10-20 years later)
Oligo or Azoospermia

Elevated temperature:
(Testis = 2.2°C ↑)
Occupational (steel mill worker, baker), febrile illness, prolonged hot bath, tight undergarment, etc.

Drugs:
(Myleran, TEM, amebicides, insecticides, etc.)

Chemicals:
(gasoline, lead fume, etc.)
Reversible (recovery: 1-3 mos.)

Varicocele:
Mostly left side
(Int. spermatic vein incompetence → → reflux of adrenal hormones into testes)

Sperm count ↓
Sperm motility ↓
Abnormal forms ↑
(tapering, precursors)
Treatment: ligation of spermatic vein

Stress:
Altered hypothalamic function
↓ GH releasing factor →
→ hypothalamic hypogonadism
= "stress pattern"
(tapering, immature form)

Nutritional factors:
Vitamin B, C deficiency
Oligospermia

Paraplegia:
Testicular atrpohy

Chronic renal failure:
Endocrine dysfunction
Testicular atrophy

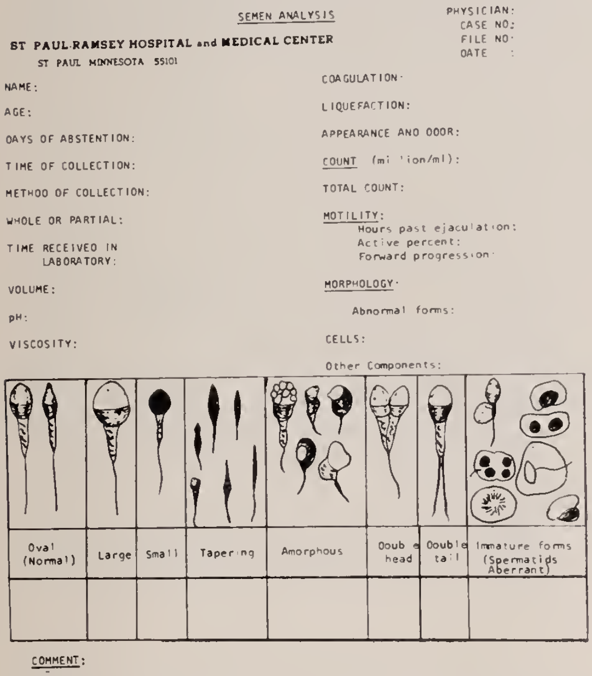
A variety of diseases, certain inherited or exogenous factors influence the quality of semen. FSH: Follicle Stimulating Hormone, LH: Luteinizing Hormone, GH: Growth Hormone, 17 KST: 17-ketosteroid.

cause of the high acidity of the vagina secretions) be a long one.

Poor sperm motility may occasionally be found in a man with normal sperm counts after a long period of continence (10 days or more). This is probably due to the deterioration of the stored cells in the ductus system.

The *morphology* of the spermatozoa should be given as much consideration as the cell count and motility. The best stain for morphologic detail is the Papanicolaou stain. It is essential that the semen smear be placed immediately into fixative (95% ethanol). Although as many as 60 different morphologic types of mature spermatozoa have been described, the classification into six or eight types as proposed by MacLeod[6,7] has practical, as well as, prospective research value (Figure 4). The form "amorphous" is used to classify all mature cells which do not fall into the other categories including the markedly degenerated forms. Every semen sample contains at least 10% abnormal sperm heads. In fertile specimen, 70% of at least 200 counted sperm should be normal (oval) in appearance.

Sperm morphology tends to vary less than do the count and motility in the same male, and may be likened to a finger print, except when some acute process (e.g. viral infection, heat exposure) produces a temporary change. Occasional specimens of poor fertility are encountered when the count and motility are excellent, and only the morphology is poor. It should be emphasized that abnormal forms can have good motility and, therefore, great care should be used to check the sperm morphology. Many correlative studies have reached the conclusion that there is no relation between poor sperm morphology and accidents of pregnancy (miscarriage, ectopic pregnancy or stillbirth). In fact, the semen quality of the husband, in a large series of these cases, is better than usual.



SEMEN ANALYSIS

ST PAUL-RAMSEY HOSPITAL and MEDICAL CENTER
ST PAUL MINNESOTA 55101

PHYSICIAN:
CASE NO:
FILE NO:
DATE :

NAME:
AGE:
DAYS OF ABSTENTION:
TIME OF COLLECTION:
METHOD OF COLLECTION:
WHOLE OR PARTIAL:
TIME RECEIVED IN LABORATORY:
VOLUME:
pH:
VISCOSITY:

COAGULATION:
LIQUEFACTION:
APPEARANCE AND ODOR:
COUNT (million/ml):
TOTAL COUNT:
MOTILITY:
Hours past ejaculation:
Active percent:
Forward progression:
MORPHOLOGY:
Abnormal forms:
CELLS:
Other Components:

Oval (Normal)	Large	Small	Tapering	Amorphous	Double head	Double tail	Immature forms (Spermatids Aberrant)

COMMENT:

Fig. 4—Semen analysis sheet: The patient age, abstention and the circumstances of collection of the specimen should be provided by the physician. The other information is filled in by the laboratory and the sheet is sent back with our appropriate comment. The morphology is analyzed according to the drawings and the percentage is indicated under each group. The sum of all except "oval" are reported as "abnormal forms."

Causes of Male Infertility

The Tables 4a, b, c summarize the important causes of male infertility[13] which can be divided into pretesticular (Table 4a), testicular (Table 4b) and post testicular (Table 4c).

TABLE 4c
Male Infertility

c) Post testicular causes: (~14%)

- Block of ducts
    - Congenital
        - Atresia of vas deferens or epididymis
        - Azoospermia (if bilateral)
    - Acquired
        - Infection
            - Gonorrheal epididymitis (most common)
                - At the tail of epididymitis
                - Frequently: Azoospermia
            - Tuberculous epididymitis
                - (following prostatic or seminal vesicle infection)
                - Frequently: Azoospermia
            - Non specific pyogenic infections
                - (from prostatitis)
                - Rarely: Azoospermia
        - Vas Ligation
            - Voluntary
            - iatrogenic
                - germinal epithelium, spermatogenesis intact; later epididymis enlarged, sperm phagocytized
- Retrograde ejaculation:
    - Disruption of internal sphincter (Figure 3)
    - Treatment: insemination with sperm recovered from bladder
- Impaired sperm motility (sperm count and testicular biopsy normal):
    - a) improper maturation of spermatozoa in epididymis (?)
    - b) biochemical abnormalities of secretions from prostate and seminal vesicles (?)

A variety of diseases, certain inherited or exogenous factors influence the quality of semen. FSH: Follicle Stimulating Hormone, LH: Luteinizing Hormone, GH: Growth Hormone, 17 KST: 17-ketosteroid.

They show clearly that a variety of abnormal conditions can influence the quality of the semen and therefore a thorough personal history and physical examination are essential.

Infertility Work-up

The infertility work-up is indicated in the absence of conception after two years of marriage in the absence of planned contraception. The male and female partners should be investigated together. For both partners the importance of a *complete and thorough history and examination* for all factors which have adverse implications (See Table 4a,b,c) cannot be overemphasized.

For the *male,* the semen analysis is the next and maybe the most important procedure. All the procedures and evaluation details have been listed previously (See "Semen Analysis" and Table 1).

Further evaluation of *female* includes basal body temperature or endometrial biopsy, histosalpingography, laporoscopy, and endocrine work-up.

The immunologic compatibility of the couple can be evaluated through the sperm agglutination test.

Acknowledgment

I am indebted to Dennis McGinley for his excellent assistance in the related work of this study.

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References

Minnesota's First Hospital—Wiggins (page 873)

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Hair Today; Gone Tomorrow

For one who has become entirely hairless in a few months, life is a "bald."

Last October, alopecia areata reared its ugly head—mine. As the months slipped by, alopecia totalis—became—total. Final alopecia universalis became a reality.

How to cope? A 64-year-old, tall, lithe, full grey-headed, family practitioner has to face the nightmare. As the months slipped by and the hairs disappeared, my close helpful medical friends tested and tested me. I was healthy—but NO hair. Everyone had a serious suggestion or theory—but no hair.

A southern winter vacation was great for my golf game, but didn't help grow hair. Razor blades—who needs them. Hair brushes—gathering dust. Mirrors were overused by my constant glances at them to see if any fuzz was developing.

Finally a visit to a world renowned alopecia expert and many more isoteric tests, biopsies and "zero" results.

Depressed—no words can express how a tall, grey haired, handsome (my own words), low handicap golfer, swinger, grandfather of five felt—awful! How to cope?

As stated earlier my medical friends tested everything. They knew and I knew no help, hope or hair.

The last resort was change my life style, run away, hide in the Montana mountains (my favorite place) or duck under the bed in the back room. No, the alopecia experts felt strongly that tensions, nerves, etc., were not the cause. No cause.

I had to cope! With this unpleasant (to me) fact—no hair. So I coped.

I went out of my way to be social, work harder, see more patients, make myself available and meet with every possible situation. It was not easy. I needed every ounce of my fighting Irish ancestry to meet what many will say is personal pride, a selfish, egotistical hang-up. Maybe—but I miss MY hair. Certainly I am the most aware I do not have a serious systemic disease nor is my hair loss a result of emotions, trauma or medication—but MY hair is gone!

*Then in the midst of all this bare period in my life—an honor—Distinguished Service Award of my State Medical Association. Face the four hundred at the Awards Banquet and make an acceptance speech—no way—but I did—I went "bare."**

In retrospect, no one has had more medical tests, exams and suggestions than I have, and all say I'm healthy—but no hair.

As a 12-year-old granddaughter says: "so Grandpa Jackie has lost his hair—so what!"

"So what," says Grandpa Jackie.

John T. Pewters, M.D.
Minneapolis, Minnesota

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*Award given at Annual Meeting in May, 1976, in Rochester.

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(Continued from page 874)

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Index to Advertisers

Allied Medical Accounts Control, Inc. 890
Anderson C. F., Co. 860
Beltone Electronics Corporation 889
Burroughs-Wellcome Co. 856
Classified Advertising 862
Finley & Friday, Inc. 852
Health Care Systems 858
Kjell Bergh's Borton Leasing, Inc. 824
Lilly, Eli & Co. 832
London Realty, Inc. 860
Medcalf Orthopedic Appliance Co. 890
Medical Protective Company 824
Minnesota Medical Seminars 828
North Central Medical Conference 854
Pharmaceutical Mfrs. Assn. 850, 851
Robins, A. H. Company 875, 876
Roche Laboratories ....Cover 2, 823, 864, 865, 866
Covers 3-4
Roerig and Company 849
Smith, Kline & French 863
Trautmans 860
U.S. Navy Recruiting District 826
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VOLUME 59 INDEX

JANUARY-DECEMBER 1976

A

A Challenge—Health Care Cost Containment. G. Roy Diessner, 557.

A Flexible and Functional Definition of Family Practice. Robert R. Thompson and Charles G. Roland, 273.

A Look at Child Health Manpower in Minnesota. Distribution and Context within the Health Planning Regions. Steven G. Thompson, Robert W. ten Bensel and Eileen A. Crowley, 580.

Acute Diabetic Complications. Bruce R. Zimmerman, 757.

Acute Phase of Myocardial Infarction. Prehospital Management of the Coronary Patient. A. A. J. Adgey, I. P. Clements, H. C. Mulholland, C. Wilson, and S. W. Webb, 347.

Adgey, A. A. J.; Clements, I. P.; Mulholland, H. C.; Wilson, C.; and Webb, S. W.: Acute Phase of Myocardial Infarction. Prehospital Management of the Coronary Patient, 347.

Adult/Geriatric Nurse Practitioners in Minnesota. Eva Anderson Vraspir, Elaine Cooley, and George Williams, 203.

Aging Eye, The. F. C. Wuest, K. D. Sayther, C. A. Carlson, and P. E. Wicklund, 540.

An Information Service for Rural Physician Associate Program Students. Gertrude Foreman, L. Yvonne Wulff, and John E. Verby, 200.

Anti-i Hemolytic Anemia in Infectious Mononucleosis. James A. Walker and Paul B. Dickinson, 301.

Asymmetric Septal Hypertrophy. Irl J. Don, 279.

Atherosclerotic Coronary—Artery Aneurysms. Report of Five Cases Diagnosed by Cine-Coronary Arteriography. Ronald Olin, David L. Duval, and D. Neil Dickson, 157.

Ausman, J. I.; Lee, M. C.; Klassen, A .C.; Seljeskog, E. L. and Chou, S. N.: Stroke: What's New? Cerebral Revascularization, 223.

B

Bamford, Joel T. M. and Bloom, Steven L.: Disseminated Gonococcemia in Plasma Cell Myeloma, 230.

Barium Demonstration of Mallory-Weiss Syndrome. Donald L. Bruns and Charles R. Nicolosi, 599.

Bernstein, Irving C.; McKelvey, John M.; and Sciarra, John J.: Twenty-Five Years of Amalgamation of Psychiatry with Obstetrics-Gynecology at the University of Minnesota, 341.

Blinding Hockey Injuries. Richard C. Horns, 255.

Bradford, David S. and Thompson, Roby C.: Fractures and Dislocations of the Spine. Indications for Surgical Intervention. 711.

Brainard, John B.: Salt Load as a Trigger for Migraine. 232.

Breitenbucher, Robert B.: The Routine Administration of the Michigan Alcoholic Screening Test to Ambulatory Patients. 425.

Briggs, Thomas G.: What's Right with Medicine? 183.

Bruhl, Heinz H.; Bauer, Henry; Levy, Barry S; Siem, Robert A.: Hepatitis-B Surface Antigen among Residents of An Institution for the Mentally Retarded. 263.

Bruns, Donald L. and Nicolosi, Charles R.: Barium Demonstration of Mallory-Weiss Syndrome. 599.

C

Calorie Intake of Patients with Advanced Cancer, the. Athanasios Theologides, Joy Ehlert, and B. J. Kennedy, 526.

Campion, Brian C.; McBride, John W.; Sukhum, Pradub and van Tyn, Robert A.: Implementation of an Expanded Emergency System. St. Paul, Minnesota Experience. 123.

Caplan, Robert H.; Kujak, Richard; Murvich, Sue; Hicks, Orville; Frank, William; and Gundersen, Gunnar A., Jr.: Current Status of the Radioactive ^{131}I Uptake Test. Effects of Gelatin Capsules and Dietary Iodine. 530.

Carroll, Richard P.: Functional Dermatochalasia. 15.

Cast Bracing of Femoral Fractures. Stephen H. McCoy, Edward M. Fitzgerald, and Kenneth A. Johnson, 58.

Causes of Death of Institutionalized Phenylketonuric (PKU) Patients—A National Survey. Robert O. Fisch, Mary K. Bilek, and Heinz H. Bruhl, 306.

Cerebellar Hemorrhage. Frederick M. Vincent, 453.

Changing Patterns of Perinatal Mortality at a Suburban Community Hospital. Sylvester J. Sanfilippo, 495.

Chemodectoma with Multiple Skeletal Metastasis and Anemia. Report of a Case. Robert A. Sweet, John F. Fairbairn, II, John W. Joyce, and John R. Goellner, 844.

Child Who Fails to Thrive—Malabsorption, the. Ralph A. Franciosi, 277.

Clinical Effects of Warm Ischemia and Prolonged Preservation on the Outcome of Transplanted Kidneys. Luis H. Toledo-Pereyra, Clive O. Callender, Allen W. Moberg, Richard L. Simmons, and John S. Najarian, 18.

Congenital Left Ventricular Diverticulum. Part of a Syndrome of Cardiac Anomalies and Midline Defects. Laura Knight, William A. Neal, Hugh J. Williams, Thomas L. Huseby, and Jesse E. Edwards, 372.

Coniff, Robert F. and Maeder, Edward C. Jr.: Management of the Pregnant Diabetic. 772.

Coronary Vein Perfusion. The History Of. Jack Kolff and W. J. Kolff, 648.

Cotton, G. E.: Diabetes Mellitus. A Plan for the Physician and His Patient. 784.

Current Status of the Radioactive ^{131}I Uptake Test. Effects of Gelatin Capsules and Dietary Iodine. Robert H. Caplan, Richard Kujak, Sue Murvich, Orville Hicks, William Frank and Gunnar A. Gundersen, Jr., 530.

D

Damsky, Leon J.; Bauer, Henry; Reeber, Erick; Shaw, James O. and Anselment, Lois A.: Human Myiasis by the Black Blow Fly. Brief Clinical and Laboratory Observations of Three Cases. 303.

Davis, Michael and Litman, Thomas: Simple Osteotomy for Hallux Valgus. 836.

Diabetes Mellitus. A Plan for the Physician and His Patient. G. E. Cotton, 784.

Diagnosis of Mild Diabetes. Frank Q. Nuttall, 747.

Diagnostic Surgical Exploration for Renal Masses. David H. Kauder and William C. DeWolf, 13.

Diarrhea in a Patient with Renal Failure. S. H. Tsai and Kenneth Preimesberger, 35.

Diessner, G. Roy: A Challenge—Health Care Cost Containment. 557.

Disseminated Gonococcemia in Plasma Cell Myeloma. Joel T. M. Bamford and Steven L. Bloom, 230.

Don, Irl J.: Asymmetric Septal Hypertrophy. 279.

Dryness of Mouth and Eyes. S. H. Tsai, 185.

E

Education of the Diabetic Patient. Carelyn P. Fylling,

E (Continued)

Judy A. Griffin, and Dee Ann E. Findley, 789.
Effect of Placebo on Exercise Response and Nitroglycerin Consumption. Keith E. Hartman, Leonard A. Nordstrom, and Fredarick L. Gobel, 839.
Encroachment on the Private Practice of Medicine. Stuart V. Thorson, 25.
Engman, Frederic J.; Campion, Brian C.; McBride, John W.; Sukhum, Pradub; and Long, Linda A.: Mobile Coronary Care in the Management of Prehospital Cardiac Arrest. St. Paul, Minnesota Experience. 833.
Erickson, Donald L.: Microsurgery for Cerebellopontine Angle Tumors. 677.
Erosion of Indian Mental Health in Cities. Joseph Westermeyer, 431.
Esophageal Moniliasis. Unusual X-Ray and Endoscopic Findings. John N. Mork, Milton W. Plucker, and Eugene J. Birkemeyer, 523.

EDITORIALS

Acute Diabetic Complications. Rudolph Ripple, 855.
Anti-i Hemolytic Anemia in Infectious Mononucleosis. Gene Hartmann, 317.
Assessment of Gestational Age. Konald Prem, 623.
Bauer, Henry: Spectrum of Agricultural Medicine. 552.
Bergstrom, William J.: Unstable Diabetes. 853.
Berman, Reuben: The Proud Profession. 463.
Blood Glucose Control in Diabetes. George F. Cahill, Jr., Donnell D. Etzwiler, and Norbert Freinkel, 803.
Cahill, George F. Jr.; Etzwiler, Donnell D.; and Freinkel, Norbert: Blood Glucose Control in Diabetes. 803.
Caloric Intake of Patients with Advanced Cancer. Neil Hoffman, 553.
Cerebellar Hemorrhage. Edward R. Laws, Jr., 464.
Chemodectoma. J. Michael Ryan, 857.
Clinical Effects of Warm Ischemia and Prolonged Preservation on the Outcome of Transplanted Kidneys. Horst Zincke, 31.
Cold Thyroid Nodule. Stanley C. Von Drashek, 465.
Cotton, G. E.: Diabetes Mellitus—1976. 799.
Dahl, Mark V.: Disseminated Gonococcal Infection. 317.
Diabetes Mellitus—1976. G. E. Cotton, 799.
Disseminated Gonococcal Infection. Mark V. Dahl, 317.
Duncan, Donald A.: Treatment of Metabolic Alkalosis with Intravenous Hydrochloric Acid. 179.
Education of the Diabetic Patient. Lois Recker, 857.
Engel, William L.: Semen Analysis and Male Fertility. 853.
Erosion of Indian Mental Health in Cities. James D. Swenson, 395.
Farley, Harrison H.: Intractable Ascites. 177.
Fehr, Peter E.: Management of the Pregnant Diabetic. 801.
Focusing on the Cause of Sudden Infant Death Syndrome. Ralph A. Franciosi, 94.
Franciosi, Ralph A.: Focusing on the Cause of Sudden Infant Death Syndrome. 94.
Functional Dermatochalasia. Robert R. Waller, 31
Galbraith, Richard F.: Transcutaneous Stimulation for Chronic Pain Relief. 855.
Gorman, Colum A.: "Silent Thyroiditis" Versus Thyrotoxicosis Factitia. 552.
Hanson, Russell F. and Thistle, Johnson L.: National Cooperative Gallstone Study. 465.
Hartmann, Gene: Anti-i Hemolytic Anemia in Infectious Mononucleosis. 317.
Haugen, John A.: Twenty-Five Years Association of a Psychiatrist. 397.
Heilman, Richard O.: Michigan Alcoholic Screening Test. 395.
Help Your Diabetic Patients. Make Them Aware of ADAM. Donald R. Moberg, 800.
Hennepin County Doctor's Directory. John E. Smith, 241.
Hepatitis B. Claus A. Pierach, 315.
Hoffman, Neil: Caloric Intake of Patients with Advanced Cancer. 553.
Hunder, Gene G.: Polymyalgia Rheumatica. 319
Intractable Ascites. Harrison H. Farley, 177.
Kostich, N. D.: Laboratory Tests in Coagulation Screening. 555.
Kragh, Lyle V.: Reduction Mammoplasty, 699.
Laboratory Tests in Coagulation Screening. N. D. Kostich, 555.
Laws, Edward R. Jr.: Cerebellar Hemorrhage. 464.
Linderholm, Bruce E.: Uterine Prolapse and Upper Urinary Tract Obstruction. 555.
Management of the Pregnant Diabetic. Peter E. Fehr, 801.
McKelvey, John M.: Transverse Myelopathy in Heroin Addiction. 175.
Michigan Alcoholic Screening Test. Richard O. Heilman, 395.
Moberg, Donald R.: Help Your Diabetic Patients. Make Them Aware of ADAM. 800.
National Cooperative Gallstone Study. Russell F. Hanson and Johnson L. Thistle, 465.
Omphaloskepsis and Other Umbilical Phenomena. Richard L. Reece, 551.
Pierach, Claus A.: Hepatitis B. 315.
Polymyalgia Rheumatica. Gene G. Hunder, 319.
Pre-Hospital Life Support as a Component of Emergency Medical Services. Roger D. White, 93.
Prem, Konald: Assessment of Gestational Age. 623.
Proud Profession, the. Reuben Berman, 463.
Recker, Loid: Education of the Diabetic Patient. 857.
Reduction Mammoplasty. Lyle V. Kragh, 699.
Reece, Richard L.: Omphaloskepsis and Other Umbilical Phenomena. 551.
Ripple, Rudolph: Acute Diabetic Complications. 855.
Ryan, J. Michael: Chemodectoma. 857.
Salovich, Elmer R.: Tennis Elbow. 465.
Semen Analysis and Male Fertility. William L. Engel, 853.
"Silent Thyroiditis" Versus Thyrotoxicosis Factitia. Colum A. Gorman, 552.
Smith, John E.: Hennepin County Doctor's Directory. 241.
Spectrum of Agricultural Medicine. Henry Bauer, 552.
Stroke: What's New? Cerebral Revascularization. Thoralf M. Sundt, Jr., 239.
Strom, Gordon W.: Urethritis Associated with Chlamydia. 243.
Sundt, Thoralf M., Jr.: Stroke: What's New? Cerebral Revascularization. 239.
Sung, Joo Ho: Two Primary Intracranial Tumors. 177.
Swenson, James D.: Erosion of Indian Mental Health in Cities. 395.
Tennis Elbow. Elmer R. Salovich, 465.
Transcutaneous Stimulation for Chronic Pain Relief. Richard F. Galbraith, 855.
Transverse Myelopathy in Heroin Addiction. John M. McKelvey, 175.
Treatment of Metabolic Alkalosis with Intravenous Hydrochloric Acid. Donald A. Duncan, 179.
Twenty-Five Years Association of a Psychiatrist. John A. Haugen, 397.
Two Primary Intracranial Tumors. Joo Ho Sung, 177.
Unstable Diabetes. William J. Bergstrom, 853.
Urethritis Associated with Chlamydia. Gordon W. Strom, 243.
Uterine Prolapse and Upper Urinary Tract Obstruction.

EDITORIALS (Continued)

Bruce E. Linderholm, 555.
Von Drashek, Stanley C.: Cold Thyroid Nodule. 465.
Waller, Robert R.: Functional Dermatochalasia. 31.
White, Roger D.: Pre-Hospital Life Support as a Component of Emergency Medical Services. 93.
Zincke, Horst: Clinical Effects of Warm Ischemia and Prolonged Preservation on the Outcome of Transplanted Kidneys. 31.

EDITOR'S NOTEBOOK

Reece, Richard L.:
  A Collection of Syndromes. (November) 741.
  bug in the belfry (July) 441.
  Editor's Report to the House of Delegates. (June) 363.
  Health Care 1976: The View from Boston. Part I. (August) 513.
  Health Care 1976. Medicine in Transition. "Change is in the Air" Part II. (September) 593.
  Health Care 1976: Medical Leadership and Social Responsibility. Part III. (October) 671.
  It Ain't Necessarily So. (May) 291.
  The Long Life in Minnesota. (April) 217.
  Social and Economic Articles. (January) 7.
  Warming Up Cold Statistics (Or: How To Talk To Floridians About Minnesota Winters). (February) 73.
  what the dickens (December) 829.
  When your tank runs low. (March) 151.

F

Farley, Harrison H.: Resection of Rhabdomyosarcoma of the Neck. An Office Procedure. 24.
Fatal Iron Poisoning in a Pregnant Female. Case Report. Robert L. Strom, Philip Schiller, Asa E. Seeds, and Robert ten Bensel, 483.
Fisch, Robert O.; Bilek, Mary K. and Bruhl, Heinz H.: Causes of Death of Institutionalized Phenylketonuric (PKU) Patients—A National Survey. 306.
Foreman, Gertrude, Wulff, L. Yvonne and Verby, John E.: An Information Service for Rural Physician Associate Program Students. 200.
Fractures and Dislocations of the Spine. Indications for Surgical Intervention. David S. Bradford and Roby C. Thompson, 711.
Franciosi, Ralph A.: The Child Who Fails to Thrive—Malabsorption. 277.
Functional Dermatochalasia. Richard P. Carroll, 15.
Fylling, Carelyn; Griffin, Judy A.; and Findley, Dee Ann E.: Education of the Diabetic Patient. 789.

G

Gobel, Fredarick L.: Role and Rationale of the Use of Propranolol in the Treatment of Patients with Angina Pectoris. 601.
Goetz, Frederick C.: Research in Human Diabetes—1976. 779.
Gonorrhea Screening in Olmsted County during 1974. G. R. Pettersen and Lyle A. Weed, 169.
Guthrie, Richard B. and Edwards, Jesse E.: Pathology of the Myxomatous Mitral Valve. Nature, Secondary Changes and Complications. 637.

H

Hair Today, Gone Tomorrow. John T. Pewters, 887.
Hargrave, Sherry A.: LATCH. 477.
Hartman, Keith E.; Nordstrom, Leonard A.; and Gobel, Fredarick L.: Effect of Placebo on Exercise Response and Nitroglycerin Consumption. 839.
Heat Stroke. Roger Ralston, 411.
Hepatitis-B Surface Antigen among Residents of An Institution for the Mentally Retarded. Heinz H. Bruhl. Henry Bauer, Barry S. Levy, and Robert A. Siem, 2
Heroics in Medicine. Carl O. Rice. 34.
Hessian Troops in the American Revolution. Their Medical and Medicinal Care. Rudolf Schmitz, 479.
Hildreth, T. A.; Stewart, William and Cass, A. S.: Uterine Prolapse and Upper Urinary Tract Obstruction. 450.
Histoplasmosis in an Elderly Female D. K. Ohrt, Editor and Mary E. Paul. Assistant Editor. 113.
Hofeldt, Fred D., Weled, Barry J.; Brown, James E.; Adler, Robert A.; Ghaed, Nasser; and Hirata, Richard M.: "Silent Thyroiditis' Versus Thyrotoxicosis Factitia. 380.
Horns, Richard C.: Blinding Hockey Injuries. 255.
Human Myiasis by the Black Blow Fly. Brief Clinical and Laboratory Observations of Three Cases. Leon J. Damsky, Henry Bauer, Erick Reeber, James O. Shaw, and Lois A. Anselment, 303.
Hyperlipoproteinemias. Current Concept. Paul Koss, 655.
Hypernephroma. A Plea for Earlier Diagnosis. Dwenda Van Veldhuizen, J. J. Tiede, and L. C. Gilman, 445.

HISTORIC HOSPITALS

Kump, Warren L.: Bedside Medical Teaching Among the Arabs. (July) 502.

I

Implementation of an Expanded Emergency System. St. Paul, Minnesota Experience. Brian C. Campion, John W. McBride, Pradub Sukhum, and Robert A. van Tyn, 123.
Infant/Preschool Hearing Impaired Child. Early Public School Intervention Emphasizing Parent Training. Winifred H. Northcott, 419.
Intractable Ascites. A New Approach. James McMillen, John P. Delaney, and Michael Levitt, 79.
Intravenous Hydrochloric Acid in the Treatment of Metabolic Alkalosis. Use in Acute Renal Failure. Robert A. Petzel, Donald S. Masler, Todd C. Miller, David C. Brown, and Robert O. Mulhausen, 166.

J

Johnson, Douglas H.: Long Term Anticoagulant Therapy Following Myocardial Infarction. 333.

K

Kauder, David H. and DeWolf, William C.: Diagnostic Surgical Exploration for Renal Masses. 13.
Key, Jack D.; Shephard, David A. E.; and Walters, Waltman: Sister Mary Joseph's Nodule and Its Relationship to Diagnosis of Carcinoma of the Umbilicus. 561.
Knight, Laura; Neal, William A.; Williams, Hugh J.; Huseby, Thomas L.; and Edwards, Jesse E.: Congenital Left Ventricular Diverticulum. Part of a Syndrome of Cardiac Anomalies and Midline Defects. 372.
Kolff, Jack and Kolff, W. J.: Coronary Vein Perfusion. The History of. 648.
Koss, Paul: Hyperlipoproteinemias. Current Concepts. 655.

L

Large Pulmonary Nodules in a Young man. Wm. A. Wilcox and C. J. Swendseen, 105.
LATCH. Sherry A. Hargrave, 477.
Arnold Lazarow, M.D. (1916-1975). Rachmiel Levine, 797.
Lee, Myoung C.; Randa, Daniel C.; Gold, Lawrence H.: Transverse Myelopathy following the Use of Heroin. 82.
Levine, Rachmiel: Arnold Lazarow, M.D. (1916-1975). 797.

L (Continued)

Long Term Anticoagulant Therapy following Myocardial Infarction. Douglas H. Johnson, 333.
Lonstein, John E.; Winter, Robert B.; Moe, John H.; Bianco, Anthony J.; Campbell, Ronald G.; and Norval, Mildred A.: School Screening for the Early Detection of Spine Deformities. Progress and Pitfalls. 51.
Lufkin, Edward G.: Management of Unstable Diabetes. 753.
Lund, Robert S. and Shafer, Rex B.: Parathyroid Adenoma Presenting as a "Cold Nodule" on Thyroid Scan. 448.

LETTERS TO THE EDITORS

Bamford, Joel T. M.: Food Allergy Test. 180.
Baker, Howard D.: Inflation and Medicine 1954-1974. (January) 33.
Bernstein, Irving C.: Twenty-Five Years Association of a Psychiatrist. (August) 556.
Carter, Earl T.: Preventive Medicine. (June) 399.
Cavazos, Lauro F. and Reich, Paul: Soviet Jewish Physicians. 243.
Coleman, James R.: Duluth Water Revised. (February) 95.
Frazier, Claude A.: Biting Insects. (July) 468.
Friedell, George: Reducing Hypercholesterolemia. 180.
Guiton, C. Richard: Minnesota Clean Indoor Air Act. (October) 701.
Janecek, James: Provider Agreements. (July) 468.
LaBar, Leah J.: On Attitudinal Barriers Towards the Physically Disabled Person. (June) 403.
Manoguerra, Anthony S.: Poison Control Center. (May) 321.
Smith, John E.: I Almost Saw a Bear. (June) 401.
Walsh, William E.: Atopic Dermatitis. (May) 321.
Wells, Arthur H.: Asbestos in Duluth Water—A Rebuttal of a Revision. (April) 244.

M

Magee, Joni: The Pelvic Examination. A View from the Other End of the Table. 99.
Management of Intra-Abdominal Henoch-Schonlein Purpura. The Role of Surgery. Luis H. Toledo-Pereyra, Thomas Von Rueden, John A. Cich, and Earl G. Yonehiro, 376.
Management of the Pregnant Diabetic. Robert F. Coniff and Edward C. Maeder, Jr., 772.
Management of Unstable Diabetes. Edward G. Lufkin, 753.
Masem, Mathias: Our Political Responsibilities as Physicians. 135.
McCoy, Stephen H.; Fitzgerald, Edward M.; and Johnson, Kenneth A.: Cast Bracing of Femoral Fractures. 58.
McDonald, Thomas W. and Fish, Charles R.: Prenatal Assessment of Intrauterine Growth Retardation. 608.
McMillen, James; Delaney, John P.; and Levitt, Michael: Intractable Ascites. A New Approach. 79.
Medical Care for an Aging Population. Implications for Medical Education. Winston R. Miller, 727.
Medical Compliance. The Effect of Appointment Reminders on Keeping Appointments in a Core City Pediatric Outpatient Department. William Meller and Arnold Anderson, 625.
Meller, William and Anderson, Arnold: Medical Compliance. The Effect of Appointment Reminders on Keeping Appointments in a Core City Pediatric Outpatient Department. 625.
Microsurgery for Cerebellopontine Angle Tumors. Donald L. Erickson, 677.
Miller, Winston R.: Medical Care for an Aging Population. Implications for Medical Education. 727.
Minnesota's First Hospital. The Practice of Medicine at Ft. Snelling 1819-1840. David S. Wiggins, 867.
Mobile Coronary Care in the Management of Prehospital Cardiac Arrest. St. Paul, Minnesota Experience. Frederic J. Engman, Brian C. Campion, John W. McBride, Pradub Sukhum and Linda A. Long, 833.
Mork, John N.; Plucker, Milton W.; Birkemeyer, Eugene J.: Esophageal Moniliasis. Unusual X-Ray and Endoscopic Findings. 523.

MINNESOTA STATE BOARD OF MEDICAL EXAMINERS

Notices of Suspension (October) 726.

MINNESOTA STATE MEDICAL ASSOCIATION

Annual Meeting—R. D. Semsch:
  And, the winner is . . . (May) 327.
  Annual Bleating . . . Not all Baa-d. (July) 494.
  Be preregistered! (January) 8.
  Education a la Carte—12 Courses Seminar Style (February) 107.
  Importance of Being Ticketed (March) 152.
  Make an Appointment with DOC (September) 630.
  Now, what was it you wanted . . . (August) 560.
  Rochester—A Celebrated City (April) 234.

MSMA HIGHLIGHTS

Division of Socio-Economic Affairs. (July) 492.
Legislation—If We Had Not Been There. (June) 407.
Looking Ahead—1977 Minnesota Legislature. (December) 859.
MINNPAC (September) 629.
Mystery of Medicaid (October) 693.
1976 MSMA Socio-Economic Conference (November) 808.
Physician's Health Forces—Let's Get Involved (August) 576.

MISCELLANEOUS

Anonsen, Richard E.: President's Address (September) 627.
Fifty Years of Faithful Service (June) 405.
Interviews—An Interview with Richard E. Anonsen, M.D., President, Minnesota State Medical Association (June) 383.
MINNESOTA MEDICINE Honor Awards (July) 469.
Minnesota State Medical Association Nominees for State Offices (April) 251.
Our Retiring Family Doctor Alta Mae Dowdell (July) 447.
President's Address. Richard E. Anonsen (September) 627.

N

Napgezek, Marvin: Reticulum Cell Sarcoma of Brain in a Patient with Chronic Lymphocytic Leukemia. 684.
Neel, Harry B.: Table Appliance for Use in Proctosigmoidoscopy. 88.
Neurologic Urinary Bladder Dysfunction. Evaluation and Treatment at the University of Minnesota. Gaylan L. Rockswold, William E. Bradley, Gerald W. Timm, and Shelley N. Chou, 687.
Northcott, Winifred H.: Infant/Preschool Hearing Impaired Child. Early Public School Intervention Emphasizing Parent Training, 419.
Nuessle, William F.; Miller, Harold E.; Norman, Franklin C.; and Vagneur, David A.: Sedimentation Rate in Polymyalgia Rheumatica. Report of 24 Cases. 297.
Nuttall, Frank Q.: Diagnosis of Mild Diabetes. 747.

O

Ohrt, D. K., Editor, and Paul, Mary E., Assistant Editor: Histoplasmosis in an Elderly Female. 113.

Olin, Ronald; Duval, David L. and Dickson, D. Neil: Artherosclerotic Coronary-Artery Aneurysms. Report of Five Cases Diagnosed by Cine-Coronary Arteriography. Ronald Olin, David L. Duval and D. Neil Dickson, 157.

Our Political Responsibilities as Physicians. Mathias Masem. 135.

P

Parathyroid Adenoma Presenting as a "Cold Nodule" on Thyroid Scan. Robert S. Lund and Rex B. Shafer, 448.

Pathology of the Myxomatous Mitral Valve. Nature, Secondary Changes and Complications. Richard B. Guthrie and Jesse E. Edwards, 637.

Pelvic Examination, the. A View from the Other End of the Table. Joni Magee, 99.

Pettersen, G. R. and Weed, Lyle A.: Gonorrhea Screening in Olmsted County During 1974. 169.

Petzel, Robert A.; Masler, Donald S.; Miller, Todd. C.; Brown, David C.; and Mulhausen, Robert O.: Intravenous Hydrochloric Acid in the Treatment of Metabolic Alkalosis. Use in Acute Renal Failure. 166.

Pewters, John T.: Hair Today; Gone Tomorrow. 887.

Philosophy of Preventive Medicine. John E. Smith, 196.

Pierach, Claus A.; Kiser, Joseph C.; and Howard, Robert B.: Thrombophlebitis. Some Practical Aspects. 164.

Posalaky, Zoltan: Semen Analysis and Male Fertility. 877.

Prenatal Assessment of Intrauterine Growth Retardation. Thomas W. McDonald and Charles R. Fish, 608.

Presurgical Coagulation Testing. John O. Swanson, 517.

Priest, James D.: Tennis Elbow. The Syndrome and A Study of Average Players, 367.

PRESIDENT'S LETTER

Anderson, Jo E.: Care with Caring. (April) 215.

Anonsen, Richard E.:
  A Tribute to Roy Diessner. (June) 361.
  Assessing Quality of Medical Care. (October) 667.
  Can I Stay in Medical School? (December) 827.
  Health Planning Law (PL. 93-641). (August) 511.
  Homicide or Death? (July) 439.
  Professional Liability. (September) 591.
  Violence on TV. (November) 739.

Bell, Donald C.: Assessing Quality of Medical Care (October) 667.

Diessner, G. Roy:
  The FTC. (March) 149.
  The Non-System. (January) 5.
  Participation in Planning. (February) 71.
  Swan Song. (May) 289.

R

Ralston, Roger: Heat Stroke. 411.

Rasmussen, Richard W. and Cole, George A.: The Spectrum of Agricultural Medicine. 536.

Reduction Mammoplasty. Carl O. Rice, 707.

Renal Transplantation in the Diabetic. David E. R. Sutherland, Carl M. Kjellstrand, Richard L. Simmons, S. Michael Mauer, Theodore J. Buselmeier, Frederick C. Goetz, Arthur J. Matas, Marvin Haymond, Richard J. Howard, John Buls, and John S. Najarian, 766.

Research in Human Diabetes—1976. Frederick G. Goetz, 779.

Resection of Rhabdomyosarcoma of the Neck. An Office Procedure. Harrison H. Farley, 24.

Reticulum Cell Sarcoma of Brain in a Patient with Chronic Lymphocytic Leukemia. Marvin Napgezek, 684.

Rice, Carl O.: Heroics in Medicine. 34.

Rice. Carl O.: Reduction Mammoplasty. 707.

Rockswold, Gaylan L.; Bradley, William E.; Timm, Gerald W.; and Chou, Shelley N.: Neurologic Urinary Bladder Dysfunction. Evaluation and Treatment at the University of Minnesota. 687.

Role and Rationale of the Use of Propranolol in the Treatment of Patients with Angina Pectoris. Fredarick L. Gobel, 601.

Routine Administration of the Michigan Alcoholic Screening Test to Ambulatory Patients, the. Robert B. Breitenbucher, 425.

S

Salt Load as a Trigger for Migraine. John B. Brainard. 232.

Sanfilippo, Sylvester J.: The Changing Patterns of Perinatal Mortality at a Suburban Community Hospital. 495.

Schmitz, Rudolf: Hessian Troops in the American Revolution. Their Medical and Medicinal Care. 479.

School Screening for the Early Detection of Spine Deformities. Progress and Pitfalls. John E. Lonstein, Robert B. Winter, John H. Moe, Anthony J. Bianco; Ronald G. Campbell, and Mildred A. Norval, 51.

Sedimentation Rate in Polymyalgia Rheumatica. Report of 24 Cases. William F. Nuessle, Harold E. Miller, Franklin C. Norman, and David A. Vagneur, 297.

Semen Analysis and Male Fertility. Zoltan Posalaky, 877.

Shapiro, Sidney K.; Segal, Marvin; and Horwitz, Charles A.: Two Primary Intracranial Tumors of Different Histological Type. Report of a Case with Both a Glioblastoma and a Meningioma. 84.

Should You Add PEP to Your Office LAB? Richard M. Steidl, 191.

Simple Osteotomy for Hallux Valgus. Michael Davis and Thomas Litman, 836.

"Silent Thyroiditis" Versus Thyrotoxicosis Factitia. Fred D. Hofeldt, Barry J. Weled, James E. Brown, Robert A. Adler, Nasser Ghaed, and Richard M. Hirata, 380.

Sister Mary Joseph's Nodule and Its Relationship to Diagnosis of Carcinoma of the Umbilicus. Jack D. Key, David A. E. Shephard, and Waltman Walters, 561.

Smith, John E.: The Philosophy of Preventive Medicine. 196.

Spectrum of Agricultural Medicine, the. Richard W. Rasmussen and George A. Cole, 536.

Steidl, Richard M.: Should You Add PEP to Your Office Lab? 191.

Stonnington, Henry H.; Stillwell, G. Keith; Ebersold, Michael J.; Thorsteinsson, Gudni; and Laws, Edward R. Jr.: Transcutaneous Electrical Stimulation for Chronic Pain Relief. 681.

Stroke: What's New? Cerebral Revascularization. J. I. Ausman, M. C. Lee, A. C. Klassen, E. L. Seljeskog, and S. N. Chou, 223.

Strom, Robert L.; Schiller, Philip; Seeds, Asa E.; and ten Bensel, Robert: Fatal Iron Poisoning in a Pregnant Female. Case Report. 483.

Sutherland, David E. R.; Kjellstrand, Carl M.; Simmons, Richard L.; Mauer, S. Michael; Buselmeier, Theodore J.; Goetz, Frederick C.; Matas, Arthur J.; Haymond, Marvin; Howard, Richard J.; Buls, John; and Najarian, John S.: Renal Transplantation in the Diabetic. 766.

Swanson, John O.: Presurgical Coagulation Testing. 517.

Swanson, John O. and Polesky, Herbert F.: Transfusion Review in Minnesota Hospitals. 188.

Sweet, Robert A.; Fairbairn, John F. II; Joyce, John W.; and Goellner, John R.: Chemodectoma with Multiple Skeletal Metastasis and Anemia. Report of a Case. 844.

T

Table Appliance for Use in Proctosigmoidoscopy. Harry B. Neel, 88.

Tennis Elbow. The Syndrome and A Study of Average Players. James D. Priest, 367.

Theologides, Athanasios; Ehlert, Joy; Kennedy, B. J.: The Calorie Intake of Patients with Advanced Cancer. 526.

Thompson, Robert R. and Roland, Charles G.: A Flexible and Functional Definition of Family Practice. 273.

Thompson, Steven G.; ten Bensel, Robert W.; and Crowley, Eileen A.: A Look at Child Health Manpower in Minnesota. Distribution and Context within the Health Planning Regions. 580.

Thorson, Stuart V.: Encroachment on the Private Practice of Medicine. 25.

Thrombophlebitis Some Practical Aspects. Claus A. Pierach, Joseph C. Kiser, and Robert B. Howard, 164.

Toledo-Pereyra, Luis H.; Callender, Clive, O.; Moberg, Allen W.; Simmons, Richard L.; and Najarian, John S.: Clinical Effects of Warm Ischemia and Prolonged Preservation on the Outcome of Transplanted Kidneys. 18.

Toledo-Pereyra, Luis H.; von Rueden, Thomas; Cich, John A.; and Yonehiro, Earl G.: Management of Intra-Abdominal Henoch-Schonlein Purpura. The Role of Surgery. 376.

Transcutaneous Electrical Stimulation for Chronic Pain Relief. A Pilot Study. Henry H. Stonnington, G. Keith Stillwell, Michael J. Ebersold, Gudni Thorsteinsson, and Edward R. Laws, Jr., 681.

Transfusion Review in Minnesota Hospitals. John O. Swanson and Herbert F. Polesky, 188.

Transverse Myelopathy Following the Use of Heroin. Myoung C. Lee, Daniel C. Randa, and Lawrence H. Gold, 82.

Tsai, S. H.: Dryness of Mouth and Eyes. 185.

Tsai, S. H. and Preimesberger, Kenneth: Diarrhea in a Patient with Renal Failure. 35.

Twenty-Five Years of Amalgamation of Psychiatry with Obstetrics-Gynecology at the University of Minnesota. Irving C. Bernstein, John M. McKelvey, and John J. Sciarra, 341.

Two Primary Intracranial Tumors of Different Histological Type. Report of a Case with Both a Glioblastoma and a Meningioma. Sidney K. Shapiro, Marvin Segal, and Charles A. Horwitz, 84.

U

Urethritis Associated with Chlamydia. Clinical and Laboratory Diagnosis. Lyle A. Weed, Thomas F. Smith, George R. Pettersen, and Joseph W. Segura, 228.

Uterine Prolapse and Upper Urinary Tract Obstruction. T. A. Hildreth, William Stewart, and A. S. Cass, 450.

V

van Veldhuizen, Dwenda; Tiede, J. J.; and Gilman, L. C.: Hypernephroma. A Plea for Earlier Diagnosis. 445.

Vincent, Frederick M.: Cerebellar Hemorrhage. 453.

Vraspir, Eva Anderson; Cooley, Elaine; and Williams, George: Adult/Geriatric Nurse Practitioners in Minnesota. 203.

W

Walker, James A. and Dickinson, Paul B.: Anti-i Hemolytic Anemia in Infectious Mononucleosis. 301.

Weed, Lyle A.; Smith, Thomas F.; Pettersen, George R.; and Segura, Joseph W.: Urethritis Associated with Chlamydia. Clinical and Laboratory Diagnosis. 228.

Westermeyer, Joseph: Erosion of Indian Mental Health in Cities. 431.

What's Right with Medicine? Thomas G. Briggs, 183.

Wiggins, David S.: Minnesota's First Hospital. The Practice of Medicine at Fort Snelling 1819-1840. 867.

Wilcox, Wm. A. and Swendseen, C. J.: Large Pulmonary Nodules in a Young Man. 105.

Wuest, F. C.; Sayther, K. D.; Carlson, C. A.; and Wicklund, P. E.: The Aging Eye. 540.

Z

Zimmerman, Bruce R.: Acute Diabetic Complications. 757.

Reminder: C.M.E. Reports Due

The Minnesota State Medical Association requires triennial reporting of continuing medical education credits as a condition of membership. The current requirement period will end on December 31, 1976. Send in your reports as soon as possible to keep your membership in good standing. Questions: Contact C.M.E. Dept., MSMA, 101 E. 5th St., St. Paul 55101.

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December 3, 1976

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Jack R. Robertson, M.D.—Santa Maria, California
Douglas R. Shanklin, M.D.—University of Chicago
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